MEMORANDUM

To: Timothy Leighton, EPA; Diana Hsieh, EPA

From: Jonathan Cohen, ICF

Date: September 29, 2016

Re: Statistical Review of the AEATF Powder and Granule Scenarios (Solid Pour Study)

Contents

1. Introduction and Summary

In April 2016, AEATF submitted the final report for their study "A Study for Measurement of Potential Dermal and Inhalation Exposure During Manual Pouring of Two Solid Formulations Containing an Antimicrobial." ICF was asked by EPA to analyze the solid pour study data to investigate the relationship between dermal and inhalation exposures and the pesticide product usage when consumers and occupational workers pour and/or scoop solid formulations of antimicrobial products. In this study, consumers poured powders or granules into a swimming pool and occupational workers poured powders or granules into a mix tank. Note that much of the SAS code used for these analyses and some of the following description was adapted from Sarkar's SAS code (which, in turn, was based on code provided by the AHETF) and his June 2010 Statistical Review "Review of Statistical Analyses in Agricultural Handler Exposure Task Force (AHETF) Monographs."

The report for the main study describes the experimental study methodology and the measurements in detail. Briefly, the study was carried out at a test site in Concord, Ohio. Monitoring of the consumers was conducted outdoors where 18 subjects separately poured granules and powders into a swimming pool. Monitoring of the occupational workers was conducted indoors where 18 subjects separately poured granules and powders into 180 gallon capacity rectangular mix tanks.

The consumer study used 18 consumer volunteers. Fourteen of these volunteers were experienced using granular or powder products or both and also lived in a home with a swimming pool within the last 5 years. One of the volunteers was experienced using granular or powder products or both but had not lived in a home with a swimming pool within

the last 5 years. Three of the volunteers were not experienced using granular or powder products or both and also had not lived in a home with a swimming pool within the last 5 years. The volunteers poured solid granules and powder containing the active ingredient cyanuric acid (CYA). The granules contained 97.6% CYA and the powder contained 95.0% CYA. Each of the 18 volunteer subjects performed a scripted task to pour granules into the swimming pool and then performed a scripted task to pour powder into the swimming pool. The original protocol design required the pouring of granules and powder to be performed by the same subject in a randomly selected order, which would avoid potential bias due to the learning experience from the first task. The final implemented design required each subject to pour the granules first and the powder second because of the potential for cross-contamination. Each volunteer was independently randomly assigned two Monitoring Event or Monitoring Experiment (ME) numbers, one for the pouring of granules and one for the pouring of powder.

For the consumers, the number and type of source containers to use, whether pre-dissolving of product was required, whether any product was to be scooped, and the number of scoops, were randomly determined and assigned to each ME prior to the start of monitoring. In order to ensure that a range of product weight was handled, each set of 18 MEs was divided into three groups of six, with the first group handling between 1 and 10 pounds; the second group handling between 10 and 20 pounds; and the third group handling between 20 and 50 pounds. Each ME handled and poured between 1 and 3 containers of product. For the pouring of granules, the MEs in group 1 were assigned source containers that were either plastic bags, 1.75 pound cans, or 6 pound cans, the MEs in group 2 were assigned 6 pound cans, and the MEs in group 3 were assigned either a 6 pound can or a 25 pound bucket. For the pouring of powder, the MEs in group 1 were assigned source containers that were either plastic bags, 1 pound cans, or 4.5 pound cans, the MEs in group 2 were assigned either 1 pound cans or 4.5 pound cans, and the MEs in group 3 were assigned either plastic bags, 1 pound cans, 4.5 pound cans, or a 25 pound bucket. Within each of groups 1 and 2, two MEs were randomly selected to pre-dissolve product in a bucket before adding it to the swimming pool. They were each given their choice of using either a plastic 2 gallon bucket or a plastic 5 gallon bucket for pre-dissolving the product. In addition to pouring product directly from containers into the pool, some of the MEs also scooped product from a 25 pound bucket into the pool. Three of the 18 powder MEs used a scoop to transfer product into the pool, while 6 of the 18 granular MEs used a scoop to transfer product into the pool. Scooping was done from the 25 pound buckets only. Two scoops were purchased for this study and provided to the subjects who were required to scoop. A red mini-hand scoop (16 oz capacity) that was 10.25 inches long (including handle) and could hold approximately 300 grams (0.66 pounds) of CYA granules was used to scoop granules. A small yellow polypropylene hand scoop (32 oz capacity) measuring 11.5 inches in length was used to scoop the powder. This scoop could hold approximately 600 grams (1.3 pounds) of powder cyanuric acid. Subjects were told how many scoops they needed to dispense into the pool. Scoops were cleaned and dried between subjects. Once the pouring was completed, the subjects were asked to place the empty container into a simulated garbage can that was located on the deck. Subjects who scooped product from a 25 pound pail were asked to place the lid back on the pail when done. If there were any spills, subjects were asked to clean up by sweeping or using the supplied water hose.

The occupational worker study used 18 volunteers. All of these volunteers were currently or previously employed in a manufacturing or industrial position where they handled granular or powder chemicals. The volunteers poured solid granules and powder containing the active ingredient cyanuric acid (CYA). The granules contained 97.6% CYA and the powder contained 95.0% CYA. Each of the 18 volunteer subjects performed a scripted task to pour granules into a mixing tank and then performed a scripted task to pour powder into a different mixing tank. The original protocol design required the pouring of granules and powder to be performed by the same subject in a randomly selected order, which would avoid potential bias due to the learning experience from the first task. The final implemented design required each subject to pour the granules first and the powder second because of the potential for cross-contamination. Each

volunteer was independently randomly assigned two Monitoring Event (ME) numbers, one for the pouring of granules and one for the pouring of powder.

For the occupational workers, the number and type of source containers to use, the amount in pounds to be poured, whether product was to be measured and weighed first or to be poured directly from the container, which of two tanks to use first, and whether to pour while standing on the ground or on a step were randomly determined and assigned to each ME prior to the start of monitoring. In order to ensure that a range of product weight was handled, each set of 18 MEs was divided into three groups of six, with the first group handling between 5 and 25 pounds; the second group handling between 26 and 50 pounds; and the third group handling between 51 and 100 pounds. In each group, one of the MEs was selected to pour directly into the tank from one or more full 25 pound containers. The remaining MEs were asked to transfer specified amounts into a bucket and pour the weighed amount into the tank. For the pouring of granules, the remaining MEs in groups 1 and 2 were assigned source containers that were either 25 pound buckets, 50 pound drums, or 90 pound drums, and the remaining MEs in group 3 were assigned 90 pound drums. For the pouring of powder, the remaining MEs in group 1 were assigned either 25 pound buckets, 50 pound drums, or 90 pound drums, and the remaining MEs in groups 2 and 3 were assigned either 50 pound drums, or 90 pound drums. Some of the MEs that poured and weighed were also selected to pour directly into the tank from one or more full 25 pound containers. Subjects weighing product were allowed to choose one of three provided scoops of different sizes. They scooped the product into a bucket and weighed the required amount on a scale. They were also each given their choice of using either a 2 gallon bucket or a 4 gallon bucket for weighing the product. Nine of the MEs in each formulation used a step while pouring into the tank and the other MEs poured while standing on the ground. Scoops were cleaned and dried between subjects. Once the pouring was completed, the subjects were asked to inspect the tank, check for spillage, and make sure the water was circulating and the product was mixing. They were then asked to close the tank lid, put the lid(s) back on the source container(s) and move them back in front of the pallet. They were also asked to inspect the area and clean up any mess.

As described above, the experimental design protocol proscribes how numerous factors are varied. For the consumers, the number and type of source containers to use, whether pre-dissolving of product was required, whether any product was to be scooped, and the number of scoops, were randomly determined and assigned to each ME prior to the start of monitoring. For the occupational workers, the number and type of source containers to use, the amount in pounds to be poured, whether product was to be measured and weighed first or to be poured directly from the container, which of two tanks to use first, and whether to pour while standing on the ground or on a step were randomly determined and assigned to each ME prior to the start of monitoring. However, the statistical analyses presented in this memorandum only use the product formulation (granules or powder), subject type (consumer or occupational worker), exposure measurements and the amounts of CYA used. We do not present analyses to estimate the impacts of other factors on exposure because population distributions for these other factors are unknown. For example, the percentage of consumers that use scoops for pool chemicals or the percentage of occupational workers that pour product directly into mixing tanks is unavailable. The goal of this analysis is to estimate the dermal and inhalation exposure for a given amount of product used, separately for the two product formulations and subject types. The other factors are therefore treated as random effects even though they were deliberately varied as part of the purposive design.

Each subject was given inner and outer dosimeters to wear and was also given a personal air-sampling pump attached to an IOM personal inhalable particulate sampler containing a glass fiber filter and a polyurethane foam (PUF) plug. The residue on the glass fiber filter measures the respirable air concentration for particles up to 4 microns in diameter. The total residue on the glass fiber filter and PUF plug measures the inhalable air concentration for particles up to 100 microns in diameter. The occupational monitoring subjects were given new chemical-resistant nitrile gloves to wear. All

subjects were given safety glasses and a dust mask to wear while pouring. The air sampling pump was switched on at the beginning of the first ME and turned off once the pouring was completed. The personal protective equipment (including the gloves for the occupational workers) was removed and the subject was escorted to the sample collection room where the samples were collected and new dosimeters were put on. The air sampling pump was switched on for the second ME and turned off once the pouring was completed. The subject was then escorted back to the sample collection room where the second set of samples were collected. The air sampling filter and PUF plug, hand wash, face/neck wipes, outer dosimeters, and inner dosimeters, were collected by a researcher and were later analyzed by the laboratory to measure the mass of CYA.

The exposure measurements were corrected for the average percentage recovery of field fortification samples. Average field fortification recoveries exceeded 100% except for the face/neck wipes which averaged 97%. Thus only the face/neck wipes were adjusted for field fortification. These analyses used the corrected measurements. An Excel spreadsheet containing the data in the report was supplied by the Study Director and used for these analyses.

The study combined data from four scenarios:

- **Consumer Granules**. Exposures to consumers pouring granules.
- **Consumer Powder**. Exposures to consumers pouring powder.
- **Occupational Granules**. Exposures to occupational workers pouring granules.
- **Occupational Powder**. Exposures to occupational workers pouring powder.

Each scenario was analyzed separately, even though each subject poured both granules and powder. Although it is plausible that data from the same subject pouring granules and powder are correlated, it is not possible to distinguish worker effects from differences between the two formulations, especially since the pouring of the powder always followed the pouring of the granules.

The dermal exposure data were used to develop exposure measurements for the following dermal exposure routes:

- **Long Dermal**. This case represents the dermal exposure to a person wearing long pants and a long-sleeved shirt, without gloves for consumer exposure and with gloves for occupational exposure. This is the sum of the mass from the six inner dosimeters, hand wash, and the face/neck wipes.
- **Short Dermal**. This case represents the dermal exposure to a person wearing short pants and a short-sleeved shirt, without gloves for consumer exposure and with gloves for occupational exposure. This is the sum of the mass from the six inner dosimeters, the outer dosimeters for the lower leg and lower arm, hand wash, and the face/neck wipes.
- **Long Short Dermal**. This case represents the dermal exposure to a person wearing long pants and a short-sleeved shirt, without gloves for consumer exposure and with gloves for occupational exposure. This is the sum of the mass from the six inner dosimeters, the outer dosimeters for the lower arm, hand wash, and the face/neck wipes.
- **Hands Only**. This case represents the dermal exposure to the hands only and is the mass from hand wash.

For the occupational workers, the hand wash measurements were taken after the gloves were removed. Measurements of CYA mass on the gloves were not made.

Inhalation exposure was measured using the total residue from the air sampling glass fiber filters and PUF plugs. Respirable inhalation exposure was measured using the residue from the air sampling glass fiber filters only. The

exposure concentration (mg/m^3) was calculated by dividing the corrected residue mass by the volume of air drawn. The following inhalation exposure metrics are analyzed in this memorandum:

- **Inhalation Concentration (mg/m^3).** Concentration measured by the glass fiber filters plus the PUF plug,
- **Inhalation Dose (mg).** Inhalation Concentration (mg/m^3) × Air Sampling Duration (hr) × Breathing Rate for Light Activity (m^3/hr). A breathing rate of 1 m^3/hr is assumed.
- **8-Hour Time Weighted Average (TWA) Inhalation Concentration (mg/m^3).** Average inhalation concentration over eight hours that includes this period of solid pouring activity.
  Inhalation Concentration (mg/m^3) × Air Sampling Duration (hr) / 8 (hr).
- **Respirable Concentration (mg/m3).** Concentration measured by the glass fiber filters only.
- **Respirable Dose (mg).** Respirable Concentration (mg/m^3) × Air Sampling Duration (hr) × Breathing Rate for Light Activity (m^3/hr). A breathing rate of 1 m^3/hr is assumed.
- **8-Hour Time Weighted Average (TWA) Respirable Concentration (mg/m^3).** Average respirable concentration over eight hours that includes this period of solid pouring activity.
  Respirable Concentration (mg/m^3) × Air Sampling Duration (hr) / 8 (hr).

For one ME (ME 9 for Consumer Granules), the dermal and inhalation exposure measurements were much higher than values for all other subjects. This was a consumer that had no experience with pouring pool chemicals and had not lived in a home with a swimming pool in the last five years. The same subject also had high exposures per pound of CYA when pouring powder (ME 17 for Consumer Powder). For each of the analyses in this memorandum we analyze the impact of removing these two potential outliers and also of removing all the data from all three subjects that had no experience with pouring pool chemicals: MEs 9, 12 and 13 for Consumer Granules and the corresponding ME numbers MEs 17, 8, and 5 for Consumer Powder. The results show that the ME 9 potential outlier had a large effect on the dermal and inhalation exposure results for Consumer Granules (excluding ME 9 reduced the arithmetic mean for short dermal by about 50%, inhalation or respirable dose or time-weighted average by about 30%). Excluding the ME 17 potential outlier for Consumer Powder had a smaller effect on the dermal and inhalation exposure results for Consumer Powder (reducing the arithmetic means by about 10 to 40 %). Excluding these two potential outliers also narrowed the confidence intervals for the summary statistics. Excluding the other two inexperienced consumers had a small effect.

Several of the measured residue values were below the level of quantitation (LOQ). Such values are called "non-detects." For most of the analyses in this memorandum, we replaced any residue value that was a non-detect by one half the LOQ. All the hand wash measurements in the study were above the LOQ of 10 µg. All but one of the face/neck wipes were above the LOQ of 10 µg; the exception was for ME 5 of Consumer Granules. For the Consumer Granules, 6 of the inner dosimeter measurements and none of the outer dosimeter measurements were below the LOQ of 3 µg. For the other scenarios, all the inner and outer dosimeters were above the LOQ. For the inhalation exposure metrics, none of the PUF plug values were below the LOQ of 0.01 µg, three of the glass fiber filter values for Consumer Granules were below the LOQ of 0.01 µg, two of the glass fiber filter values for Consumer Powder were below the LOQ of 0.01 µg, and none of the glass fiber filter values were below the LOQ for Occupational Granules or Powder. In Table 19, Table 20, Table 37 and Table 38 below, we present the results of alternative analyses of values below the LOQ that demonstrate that the impact of the non-detects is small using any of the statistical methods used to analyze non-detects.

In this memorandum we present the analysis of the unit or normalized exposure defined as the dermal or inhalation exposure divided by the pounds of active ingredient handled. Estimates of the arithmetic and geometric means and standard deviation as well as the 95th percentile are computed using the empirical data as well as a lognormal simple

random sampling model. Unlike some of the other studies previously analyzed, we did not use lognormal mixed models since there are no cluster or random effects. Each scenario is treated as a separate simple random sample. The empirical model calculates statistics for all the unit exposure measurements assuming the data are statistically independent. The lognormal simple random sampling model calculates statistics for all the unit exposure measurements, assuming the unit exposure measurements are statistically independent with a lognormal distribution.

For each summary statistic we present confidence intervals. We also compute the fold relative accuracies of the summary statistics and compare them with the (primary) study design benchmark of 3-fold accuracy, which was generally met for the various arithmetic mean and 95^{th} percentile estimates, except for the dermal exposure estimates for the Consumer Granules scenario and for the empirical 95^{th} percentile. To evaluate the statistical models we present quantile-quantile plots of the data to determine whether the normalized exposure should be treated as being normally or lognormally distributed.

The statistical models for the normalized exposure assume that the mean value of the logarithm of the exposure is equal to an intercept plus the slope times the logarithm of the amount of active ingredient used, where the slope equals 1. To test this "log-log-linearity with a slope of 1" assumption, the lognormal simple random sampling model with a slope term was fitted to the data and a 95% confidence interval for the slope was calculated. A statistical test was used to determine if the slope was 1 or 0, corresponding either to a valid normalized exposure model or to a case where the exposure is independent of the amount of active ingredient used. We applied this test to each exposure metric using the lognormal simple random sampling model. We also present quantile-quantile plots of the residuals from the lognormal simple random sampling model with a slope term to evaluate the fitted models. We also evaluated quadratic regression models.

For Consumer Granules, the dermal exposure slopes range from about 0.3 to 0.5 and, using all the data, the confidence intervals for the slope include 0 but (in most cases) not 1. Thus the assumption of independence was not rejected and the assumption of log-log-linearity with slope 1 was rejected. For inhalation exposures using Consumer Granules, the slopes are about 0.8 and in most cases the confidence intervals for the slope include 1 but not 0. Thus the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was not rejected. For dermal and inhalation exposures using Consumer Powder, the slopes range from 0.3 to 0.8 and the confidence intervals do not include 0; the intervals include 1 in about half the cases. Thus the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was rejected in about half of the cases. For dermal and inhalation exposures using Occupational Granules, most of the slopes were above 1 (ranging from about 0.9 to 1.7) and the confidence intervals include 1 but not 0. Thus the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was not rejected. For dermal and inhalation exposures using Occupational Powder, most of the slopes were below 1 (ranging from 0.4 to 1.1) and the confidence intervals mostly include 1 but not 0. Thus the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was not rejected.

A secondary objective is for meeting 80% power for detecting log-log-linearity with a slope of 1. This objective is approximately met if the widths of the confidence intervals for the slope based on the lognormal model are at most 1.4. The results show that the observed widths are all below 1.4 for the Consumer Scenarios but exceed 1.4 for about half of the cases for the Occupational Granules and Occupational Powder scenarios. The maximum width was 1.77 for the hands only exposure route for Occupational Powder. Therefore the secondary objective of meeting 80% power for detecting proportionality was not met for the Occupational Granules and Occupational Powder scenarios.

2. Summary Statistics of Exposure per Pound of Active Ingredient Handled

Table 1 to Table 14 summarize the normalized exposure data (per lb active ingredient handled) with the summary statistics from the 18 measurements for each scenario and each dermal and inhalation exposure route. These analyses assume that the exposure measurements within each subset come from some unspecified distribution for that subset. For the Consumer Granules and Consumer Powder scenarios, results are provided for all 18 measurements ("All") and for two subsets after excluding potential outliers or inexperienced consumers. The subset "Exc. ME 9" excludes the high outlier value for Consumer Granules ME 9 noted in the study report. The subset "Exc. ME 17" excludes the high outlier value for Consumer Powder ME 17 noted in the study report that was for the same subject as ME 9 for Consumer Granules; this value was not treated as an outlier in the study report. This subject had no experience in using granular or powder pool chemicals. The subset "Experienced" only includes the 15 subjects that reported experience in using granular or powder pool chemicals. We include this subset to help evaluate the possibility that the high results for Consumer Granules ME 9 / Consumer Powder ME 17 are explicable due to the lack of experience of that subject. For the Occupational Granules and Occupational Powder scenarios, all subjects reported experience (this was part of the recruitment procedure) and no exclusions were evaluated.

Table 1. Summary statistics for Consumer normalized long dermal exposure (mg/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	1.348	0.535	0.568	3.683	2.134	2.098
Arithmetic Standard Deviation	3.686	1.343	1.432	6.834	1.927	1.930
Geometric Mean	0.199	0.154	0.142	1.620	1.364	1.349
Geometric Standard Deviation	5.712	4.088	4.404	3.405	2.761	2.741
Min	0.027	0.027	0.027	0.328	0.328	0.328
5%	0.027	0.027	0.027	0.328	0.328	0.328
10%	0.030	0.030	0.030	0.372	0.372	0.372
25%	0.052	0.052	0.049	0.517	0.517	0.517
50%	0.120	0.111	0.091	1.484	0.985	0.985
75%	0.547	0.374	0.547	4.262	3.523	3.523
90%	5.671	0.785	0.785	5.845	5.752	5.752
95%	15.162	5.671	5.671	30.022	5.845	5.845
Max	15.162	5.671	5.671	30.022	5.845	5.845

Table 2. Summary statistics for Consumer normalized short dermal exposure (mg/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	2.937	1.534	1.673	10.494	8.706	9.383
Arithmetic Standard Deviation	7.431	4.584	4.883	19.672	18.709	19.867
Geometric Mean	0.490	0.387	0.376	4.299	3.766	4.032
Geometric Standard Deviation	5.143	3.811	4.157	3.551	3.224	3.216
Min	0.048	0.048	0.048	0.639	0.639	0.639
5%	0.048	0.048	0.048	0.639	0.639	0.639
10%	0.076	0.076	0.076	0.786	0.786	0.956
25%	0.230	0.230	0.213	1.514	1.514	1.514
50%	0.360	0.334	0.251	5.238	5.223	5.223
75%	0.732	0.616	0.732	7.176	6.551	7.176
90%	19.277	1.339	1.339	40.886	8.815	8.815
95%	26.788	19.277	19.277	80.527	80.527	80.527
Max	26.788	19.277	19.277	80.527	80.527	80.527

Table 3. Summary statistics for Consumer normalized long short dermal exposure (mg/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	1.665	0.617	0.653	5.260	3.356	3.402
Arithmetic Standard Deviation	4.652	1.423	1.517	8.623	3.111	3.196
Geometric Mean	0.288	0.224	0.212	2.556	2.182	2.237
Geometric Standard Deviation	5.119	3.624	3.910	3.277	2.743	2.699
Min	0.032	0.032	0.032	0.386	0.386	0.386
5%	0.032	0.032	0.032	0.386	0.386	0.386
10%	0.033	0.033	0.033	0.602	0.602	0.685
25%	0.108	0.108	0.107	0.904	0.904	0.904
50%	0.187	0.184	0.182	2.801	2.370	2.370
75%	0.572	0.418	0.572	5.421	5.010	5.010
90%	6.054	0.950	0.950	12.212	6.736	6.736
95%	19.467	6.054	6.054	37.626	12.212	12.212
Max	19.467	6.054	6.054	37.626	12.212	12.212

Table 4. Summary statistics for Consumer normalized hands only dermal exposure (mg/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	1.305	0.502	0.534	3.302	1.858	1.817
Arithmetic Standard Deviation	3.639	1.311	1.398	6.371	1.797	1.810
Geometric Mean	0.162	0.124	0.114	1.335	1.117	1.087
Geometric Standard Deviation	6.325	4.497	4.847	3.669	2.970	2.985
Min	0.022	0.022	0.022	0.204	0.204	0.204
5%	0.022	0.022	0.022	0.204	0.204	0.204
10%	0.025	0.025	0.025	0.299	0.299	0.299
25%	0.041	0.041	0.040	0.487	0.487	0.404
50%	0.089	0.079	0.068	1.178	0.821	0.821
75%	0.468	0.344	0.468	3.245	2.786	2.786
90%	5.520	0.760	0.760	5.664	5.409	5.409
95%	14.965	5.520	5.520	27.854	5.664	5.664
Max	14.965	5.520	5.520	27.854	5.664	5.664

Table 5. Summary statistics for Consumer normalized inhalation concentration exposure ((mg/m^3)/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	0.040	0.038	0.041	1.397	1.172	1.309
Arithmetic Standard Deviation	0.033	0.033	0.035	2.727	2.633	2.784
Geometric Mean	0.028	0.026	0.027	0.501	0.437	0.506
Geometric Standard Deviation	2.557	2.552	2.669	3.724	3.366	3.385
Min	0.004	0.004	0.004	0.112	0.112	0.112
5%	0.004	0.004	0.004	0.112	0.112	0.112
10%	0.009	0.009	0.009	0.119	0.119	0.119
25%	0.014	0.014	0.014	0.206	0.206	0.229
50%	0.027	0.026	0.026	0.389	0.373	0.405
75%	0.065	0.056	0.065	1.027	0.684	1.027
90%	0.090	0.090	0.090	5.228	2.018	2.018
95%	0.122	0.122	0.122	11.132	11.132	11.132
Max	0.122	0.122	0.122	11.132	11.132	11.132

Table 6. Summary statistics for Consumer normalized inhalation dose exposure (mg/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	0.00287	0.00199	0.00182	0.04408	0.03642	0.04015
Arithmetic Standard Deviation	0.00422	0.00207	0.00212	0.05490	0.04562	0.04745
Geometric Mean	0.00158	0.00137	0.00122	0.02491	0.02221	0.02530
Geometric Standard Deviation	2.96391	2.53575	2.53549	2.87935	2.63382	2.60092
Min	0.00014	0.00014	0.00014	0.00674	0.00674	0.00674
5%	0.00014	0.00014	0.00014	0.00674	0.00674	0.00674
10%	0.00043	0.00043	0.00043	0.00705	0.00705	0.00746
25%	0.00095	0.00095	0.00087	0.00991	0.00991	0.00991
50%	0.00154	0.00150	0.00136	0.02489	0.02304	0.02674
75%	0.00226	0.00203	0.00187	0.03419	0.03364	0.03419
90%	0.00902	0.00427	0.00301	0.17428	0.10271	0.10271
95%	0.01777	0.00902	0.00902	0.18553	0.18553	0.18553
Max	0.01777	0.00902	0.00902	0.18553	0.18553	0.18553

Table 7. Summary statistics for Consumer normalized inhalation time-weighted average concentration exposure ((mg/m^3)/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	0.00036	0.00025	0.00023	0.00551	0.00455	0.00502
Arithmetic Standard Deviation	0.00053	0.00026	0.00026	0.00686	0.00570	0.00593
Geometric Mean	0.00020	0.00017	0.00015	0.00311	0.00278	0.00316
Geometric Standard Deviation	2.96391	2.53575	2.53549	2.87935	2.63382	2.60092
Min	0.00002	0.00002	0.00002	0.00084	0.00084	0.00084
5%	0.00002	0.00002	0.00002	0.00084	0.00084	0.00084
10%	0.00005	0.00005	0.00005	0.00088	0.00088	0.00093
25%	0.00012	0.00012	0.00011	0.00124	0.00124	0.00124
50%	0.00019	0.00019	0.00017	0.00311	0.00288	0.00334
75%	0.00028	0.00025	0.00023	0.00427	0.00421	0.00427
90%	0.00113	0.00053	0.00038	0.02178	0.01284	0.01284
95%	0.00222	0.00113	0.00113	0.02319	0.02319	0.02319
Max	0.00222	0.00113	0.00113	0.02319	0.02319	0.02319

Table 8. Summary statistics for Consumer normalized respirable concentration exposure ((mg/m^3)/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	0.0009590	0.0009305	0.0009960	0.0031835	0.0027223	0.0028735
Arithmetic Standard Deviation	0.0007221	0.0007339	0.0007587	0.0039117	0.0034916	0.0036790
Geometric Mean	0.0006970	0.0006678	0.0007075	0.0014864	0.0013211	0.0013551
Geometric Standard Deviation	2.4165828	2.4352406	2.5427011	3.6686551	3.4443103	3.5723589
Min	0.0001616	0.0001616	0.0001616	0.0002501	0.0002501	0.0002501
5%	0.0001616	0.0001616	0.0001616	0.0002501	0.0002501	0.0002501
10%	0.0001721	0.0001721	0.0001721	0.0003240	0.0003240	0.0003240
25%	0.0003660	0.0003660	0.0002449	0.0004883	0.0004883	0.0004883
50%	0.0008607	0.0007984	0.0009230	0.0009041	0.0008157	0.0008157
75%	0.0014427	0.0014111	0.0014569	0.0047882	0.0034460	0.0047882
90%	0.0023709	0.0023709	0.0023709	0.0110226	0.0096338	0.0096338
95%	0.0025673	0.0025673	0.0025673	0.0121688	0.0121688	0.0121688
Max	0.0025673	0.0025673	0.0025673	0.0121688	0.0121688	0.0121688

Table 9. Summary statistics for Consumer normalized respirable dose exposure (mg/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	0.0000653	0.0000480	0.0000410	0.0001208	0.0001063	0.0001069
Arithmetic Standard Deviation	0.0000876	0.0000488	0.0000397	0.0001279	0.0001155	0.0001197
Geometric Mean	0.0000397	0.0000349	0.0000317	0.0000738	0.0000672	0.0000678
Geometric Standard Deviation	2.5003010	2.1277732	1.9705432	2.8052021	2.6639795	2.6295717
Min	0.0000103	0.0000103	0.0000103	0.0000208	0.0000208	0.0000208
5%	0.0000103	0.0000103	0.0000103	0.0000208	0.0000208	0.0000208
10%	0.0000133	0.0000133	0.0000133	0.0000210	0.0000210	0.0000210
25%	0.0000243	0.0000243	0.0000242	0.0000294	0.0000294	0.0000294
50%	0.0000306	0.0000305	0.0000300	0.0000725	0.0000579	0.0000579
75%	0.0000470	0.0000428	0.0000428	0.0001723	0.0001606	0.0001606
90%	0.0001715	0.0001707	0.0000790	0.0003674	0.0002028	0.0002028
95%	0.0003607	0.0001715	0.0001715	0.0004788	0.0004788	0.0004788
Max	0.0003607	0.0001715	0.0001715	0.0004788	0.0004788	0.0004788

Table 10. Summary statistics for Consumer normalized respirable time-weighted average concentration exposure ((mg/m^3)/lb AI) using empirical sampling model

Statistic	Granules All	Granules Exc. ME 9	Granules Experienced	Powder All	Powder Exc. ME 17	Powder Experienced
Arithmetic Mean	0.0000082	0.0000060	0.0000051	0.0000151	0.0000133	0.0000134
Arithmetic Standard Deviation	0.0000110	0.0000061	0.0000050	0.0000160	0.0000144	0.0000150
Geometric Mean	0.0000050	0.0000044	0.0000040	0.0000092	0.0000084	0.0000085
Geometric Standard Deviation	2.5003010	2.1277732	1.9705432	2.8052021	2.6639795	2.6295717
Min	0.0000013	0.0000013	0.0000013	0.0000026	0.0000026	0.0000026
5%	0.0000013	0.0000013	0.0000013	0.0000026	0.0000026	0.0000026
10%	0.0000017	0.0000017	0.0000017	0.0000026	0.0000026	0.0000026
25%	0.0000030	0.0000030	0.0000030	0.0000037	0.0000037	0.0000037
50%	0.0000038	0.0000038	0.0000038	0.0000091	0.0000072	0.0000072
75%	0.0000059	0.0000053	0.0000053	0.0000215	0.0000201	0.0000201
90%	0.0000214	0.0000213	0.0000099	0.0000459	0.0000254	0.0000254
95%	0.0000451	0.0000214	0.0000214	0.0000599	0.0000599	0.0000599
Max	0.0000451	0.0000214	0.0000214	0.0000599	0.0000599	0.0000599

Table 11. Summary statistics for Occupational Granules normalized dermal exposure (mg/lb AI) using empirical sampling model

Statistic	Long Dermal	Short Dermal	Long Short Dermal	Hands Only
Arithmetic Mean	0.048	0.602	0.439	0.013
Arithmetic Standard Deviation	0.030	0.441	0.393	0.011
Geometric Mean	0.039	0.467	0.295	0.010
Geometric Standard Deviation	1.946	2.150	2.686	2.280
Min	0.009	0.083	0.034	0.002
5%	0.009	0.083	0.034	0.002
10%	0.015	0.207	0.057	0.003
25%	0.028	0.263	0.145	0.007
50%	0.040	0.467	0.288	0.013
75%	0.057	0.824	0.642	0.017
90%	0.096	1.127	1.037	0.020
95%	0.128	1.814	1.534	0.048
Max	0.128	1.814	1.534	0.048

Table 12. Summary statistics for Occupational Granules normalized inhalation and respirable exposure (mg/lb AI for dose, (mg/m3)/lb AI for concentration) using empirical sampling model

Statistic	Inhalation Conc	Inhalation Dose	Inhalation TWA Conc	Respirable Conc	Respirable Dose	Respirable TWA Conc
Arithmetic Mean	0.671	0.07008	0.00876	0.0261977	0.0028466	0.0003558
Arithmetic Standard Deviation	0.674	0.06814	0.00852	0.0209333	0.0023431	0.0002929
Geometric Mean	0.451	0.04493	0.00562	0.0186774	0.0018622	0.0002328
Geometric Standard Deviation	2.638	2.87333	2.87333	2.4988762	2.8631141	2.8631141
Min	0.044	0.00512	0.00064	0.0033257	0.0002707	0.0000338
5%	0.044	0.00512	0.00064	0.0033257	0.0002707	0.0000338
10%	0.110	0.00592	0.00074	0.0044787	0.0003732	0.0000467
25%	0.279	0.02412	0.00301	0.0081196	0.0007301	0.0000913
50%	0.511	0.04154	0.00519	0.0247279	0.0019730	0.0002466
75%	0.735	0.10740	0.01342	0.0309077	0.0047638	0.0005955
90%	1.760	0.14665	0.01833	0.0664813	0.0066017	0.0008252
95%	2.849	0.28494	0.03562	0.0801714	0.0080171	0.0010021
Max	2.849	0.28494	0.03562	0.0801714	0.0080171	0.0010021

Table 13. Summary statistics for Occupational Powder normalized dermal exposure (mg/lb AI) using empirical sampling model

Statistic	Long Dermal	Short Dermal	Long Short Dermal	Hands Only
Arithmetic Mean	0.207	3.063	2.291	0.064
Arithmetic Standard Deviation	0.124	2.402	1.907	0.063
Geometric Mean	0.159	2.198	1.455	0.035
Geometric Standard Deviation	2.310	2.479	3.088	3.543
Min	0.031	0.324	0.142	0.005
5%	0.031	0.324	0.142	0.005
10%	0.044	0.504	0.172	0.007
25%	0.067	1.122	0.823	0.012
50%	0.224	2.600	2.056	0.052
75%	0.311	4.149	3.448	0.088
90%	0.383	8.283	5.576	0.159
95%	0.409	8.635	6.959	0.227
Max	0.409	8.635	6.959	0.227

Table 14. Summary statistics for Occupational Powder normalized inhalation and respirable exposure (mg/lb AI for dose, (mg/m3)/lb AI for concentration) using empirical sampling model

Statistic	Inhalation Conc	Inhalation Dose	Inhalation TWA Conc	Respirable Conc	Respirable Dose	Respirable TWA Conc
Arithmetic Mean	1.398	0.20452	0.02556	0.0108411	0.0016640	0.0002080
Arithmetic Standard Deviation	0.971	0.17988	0.02249	0.0101096	0.0018710	0.0002339
Geometric Mean	1.040	0.13519	0.01690	0.0075973	0.0009875	0.0001234
Geometric Standard Deviation	2.319	2.73564	2.73564	2.4002823	2.9562899	2.9562899
Min	0.296	0.02073	0.00259	0.0014654	0.0001559	0.0000195
5%	0.296	0.02073	0.00259	0.0014654	0.0001559	0.0000195
10%	0.333	0.03162	0.00395	0.0027670	0.0001710	0.0000214
25%	0.452	0.05276	0.00659	0.0038393	0.0005026	0.0000628
50%	1.215	0.16940	0.02117	0.0088605	0.0012317	0.0001540
75%	2.240	0.27323	0.03415	0.0138945	0.0017943	0.0002243
90%	2.889	0.48142	0.06018	0.0269144	0.0062428	0.0007804
95%	2.889	0.68703	0.08588	0.0416188	0.0065843	0.0008230
Max	2.889	0.68703	0.08588	0.0416188	0.0065843	0.0008230

The summary statistics in Table 2 show that excluding ME 9 for Consumer Granules reduced the arithmetic mean for short dermal by about 50%, and a very similar reduction arises from removing all three inexperienced consumers. The summary statistics in Table 2 also show that excluding ME 17 for Consumer Powder reduced the arithmetic mean for short dermal by about 20%, and a similar reduction of about 10% arises from removing all three inexperienced consumers. For the other three dermal exposure metrics, reductions of about 50% arise for Consumer Granules and reductions of about 40% arise for Consumer Powder. The summary statistics in Tables 5 and 8 show that excluding ME 9 for Consumer Granules reduced the arithmetic means for inhalation or respirable concentration by about 5%, and a very similar reduction arises from removing all three inexperienced consumers. The summary statistics in Tables 6, 7, 9 and 10 show that excluding ME 9 for Consumer Granules reduced the arithmetic means for inhalation or respirable dose or time-weighted average concentration by about 30%, and a very similar reduction arises from removing all three inexperienced consumers. Excluding the ME 17 for Consumer Powder reduced the arithmetic meansfor the inhalation exposure metrics by about 15%, but a small increase or decrease arises from removing all three inexperienced consumers. These findings suggest that ME 9 for Consumer Granules and ME 17 for Consumer Powder are potential outliers, but this is associated with the “messiness” of that particular subject and is not solely because of inexperience with pouring granular or powder chemicals.

The results also show the proportion of the dermal exposure from hands only. Based on the arithmetic means, the percentages of exposure from hands only for Consumer Granules are about 97% of the Long Dermal (94% excluding ME 9), and 44% of Short Dermal (33% excluding ME 9). The percentages of exposure from hands only for Consumer Powder are about 90% of the Long Dermal (87% excluding ME 17), and 31% of Short Dermal (21% excluding ME 17). The percentages of exposure from hands only for Occupational Granules are about 37% of the Long Dermal and 2% of Short Dermal. The percentages of exposure from hands only for Occupational Powder are about 31% of the Long Dermal and

2% of Short Dermal. The much lower percentages for the Occupational Granules and Powder scenarios are due to the fact that the consumers did not wear gloves and the occupational workers wore gloves.

3. Statistical Models

The statistical analyses of the normalized exposure use the following two alternative statistical models. Let X be the normalized exposure and X = exp(Y) so that Y = log (X), where log denotes the natural logarithm. LnGM is the log of the geometric mean. Let Z95 be the 95th percentile of a standard normal distribution, approximately 1.645.

- Empirical simple random sampling model. Code "s." Assumes that all the values of X were randomly drawn from an unspecified distribution. Gives empirical estimates such as in Tables 1 to 14 above.
  - Y = LnGM + Error. Error is independent and identically distributed with mean 0 and the same variance for every measurement.
  - AMs = Arithmetic mean of X values
  - GMs = Geometric mean of X values = exp(LnGM) (= GMu)
  - GSDs = Geometric standard deviation of X values (= GSDu)
  - P95s = 95th percentile of X values
- Lognormal simple random sampling model. Code "u." Assumes that all the values of X were randomly drawn from a lognormal distribution.
  - Y = LnGM + Error. Error is normally distributed with mean 0, variance Vu, and standard deviation Su = √Vu.
  - AMu = Modeled arithmetic mean of X values = exp(LnGM) exp(½ Vu)
  - GMu = Modeled geometric mean of X values = exp(LnGM)
  - GSDu = Modeled geometric standard deviation of X values = exp(Su)
  - P95u = Modeled 95th percentile of X values = exp(LnGM) exp(Z95×Su)

Table 15 to Table 18 present the arithmetic mean and 95th percentile estimates from the lognormal simple random sampling model, together with 95% confidence intervals, for all the exposure routes and for the various data subsets. These are the values of AMu and P95u. The other summary statistics are presented in more detail below. The data set "Exc. ME 9" is the 17 subjects from the Consumer Granules data excluding the potential outlier ME 9. The data set "Exc. ME 17" is the 17 subjects from the Consumer Powder data excluding the potential outlier ME 17. The data set "Experienced" for Consumer Granules and Consumer Powder are the 15 subjects with some experience of using granular or powder pool chemicals. All of the Occupational Granules and Occupational Powder data were for subjects with occupational experience of using granular or powder chemicals.

Table 15. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Consumer Granules

Exposure Route	Clothing	Data Set	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	All	0.906 (0.271, 3.271)	3.489 (0.979, 12.023)
		Exc. ME 9	0.415 (0.169, 1.152)	1.560 (0.547, 4.324)
		Experienced	0.428 (0.153, 1.390)	1.632 (0.504, 5.146)
	Short Dermal	All	1.874 (0.624, 6.668)	7.248 (2.196, 23.179)
		Exc. ME 9	0.948 (0.412, 2.422)	3.499 (1.293, 9.219)
		Experienced	1.038 (0.394, 3.138)	3.918 (1.266, 11.812)
	Long Short Dermal	All	1.091 (0.365, 3.856)	4.219 (1.283, 13.450)
		Exc. ME 9	0.514 (0.232, 1.245)	1.865 (0.716, 4.739)
		Experienced	0.537 (0.216, 1.505)	1.995 (0.676, 5.736)
	Hands Only	All	0.890 (0.238, 4.247)	3.374 (0.879, 12.497)
		Exc. ME 9	0.385 (0.108, 1.432)	1.476 (0.326, 5.356)
		Experienced	0.395 (0.128, 1.453)	1.523 (0.436, 5.171)
Inhalation Concentration (mg/m^3/lb AI)		All	0.043 (0.026, 0.074)	0.130 (0.065, 0.252)
		Exc. ME 9	0.041 (0.024, 0.070)	0.122 (0.061, 0.241)
		Experienced	0.044 (0.025, 0.084)	0.138 (0.063, 0.294)
Inhalation Dose (mg/lb AI)		All	0.00284 (0.00153, 0.00552)	0.00941 (0.00426, 0.02035)
		Exc. ME 9	0.00211 (0.00125, 0.00363)	0.00631 (0.00316, 0.01238)
		Experienced	0.00189 (0.00109, 0.00340)	0.00566 (0.00270, 0.01163)
Inhalation 8-hr TWA (mg/m^3/lb AI)		All	0.00036 (0.00019, 0.00069)	0.00118 (0.00053, 0.00254)
		Exc. ME 9	0.00026 (0.00016, 0.00045)	0.00079 (0.00039, 0.00155)
		Experienced	0.00024 (0.00014, 0.00043)	0.00071 (0.00034, 0.00145)
Respirable Concentration (mg/m^3/lb AI)		All	0.00103 (0.00064, 0.00169)	0.00298 (0.00156, 0.00557)

Exposure Route	Clothing	Data Set	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
		Exc. ME 9	0.00099 (0.00061, 0.00166)	0.00289 (0.00149, 0.00550)
		Experienced	0.00109 (0.00063, 0.00197)	0.00328 (0.00157, 0.00677)
Respirable Dose (mg/lb AI)		All	0.0000604 (0.0000368, 0.0001017)	0.0001793 (0.0000919, 0.0003436)
		Exc. ME 9	0.0000464 (0.0000309, 0.0000705)	0.0001208 (0.0000689, 0.0002086)
		Experienced	0.0000398 (0.0000274, 0.0000589)	0.0000966 (0.0000564, 0.0001634)
Respirable 8-hr TWA (mg/m^3/lb AI)		All	0.0000076 (0.0000046, 0.0000127)	0.0000224 (0.0000115, 0.0000430)
		Exc. ME 9	0.0000058 (0.0000039, 0.0000088)	0.0000151 (0.0000086, 0.0000261)
		Experienced	0.0000050 (0.0000034, 0.0000074)	0.0000121 (0.0000071, 0.0000204)

Table 16. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Consumer Powder

Exposure Route	Clothing	Data Set	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	All	3.431 (1.638, 7.738)	12.154 (4.979, 29.303)
		Exc. ME 17	2.284 (1.284, 4.318)	7.248 (3.387, 15.406)
		Experienced	2.242 (1.237, 4.294)	7.081 (3.173, 15.416)
	Short Dermal	All	9.595 (4.414, 22.537)	34.557 (13.733, 85.849)
		Exc. ME 17	7.471 (3.718, 16.370)	25.824 (10.743, 61.591)
		Experienced	7.977 (3.877, 17.873)	27.544 (10.866, 67.849)
	Long Short Dermal	All	5.169 (2.551, 11.196)	18.006 (7.585, 42.230)

Exposure Route	Clothing	Data Set	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
		Exc. ME 17	3.630 (2.050, 6.826)	11.473 (5.386, 24.271)
		Experienced	3.662 (2.046, 6.929)	11.453 (5.195, 24.639)
	Hands Only	All	3.109 (1.393, 7.569)	11.333 (4.397, 28.827)
		Exc. ME 17	2.020 (1.037, 3.241)	6.694 (3.005, 10.957)
		Experienced	1.976 (1.022, 4.112)	6.568 (2.749, 15.274)
Inhalation Concentration (mg/m^3/lb AI)		All	1.190 (0.526, 2.927)	4.360 (1.673, 11.209)
		Exc. ME 17	0.912 (0.440, 2.091)	3.216 (1.295, 7.921)
		Experienced	1.064 (0.494, 2.523)	3.760 (1.424, 9.636)
Inhalation Dose (mg/lb AI)		All	0.04357 (0.02380, 0.08308)	0.14184 (0.06566. 0.30314)
		Exc. ME 17	0.03550 (0.02067, 0.06452)	0.10925 (0.05288, 0.022425)
		Experienced	0.03995 (0.02295, 0.07318)	0.12187 (0.05693, 0.25484)
Inhalation 8-hr TWA (mg/m^3/lb AI)		All	0.00545 (0.00298, 0.01039)	0.01773 (0.00821, 0.03789)
		Exc. ME 17	0.00444 (0.00258, 0.00806)	0.01366 (0.00661, 0.02803)
		Experienced	0.00499 (0.00287, 0.00915)	0.01523 (0.00712, 0.03186)
Respirable Concentration (mg/m^3/lb AI)		All	0.00346 (0.00155, 0.00842)	0.01261 (0.00489, 0.03207)
		Exc. ME 17	0.00284 (0.00134, 0.00666)	0.01010 (0.00400, 0.02531)
		Experienced	0.00305 (0.00135, 0.00765)	0.01100 (0.00399, 0.02939)
Respirable Dose (mg/lb AI)		All	0.0001257 (0.0000700, 0.002343)	0.0004028 (0.0001900, 0.0008449)
		Exc. ME 17	0.0001086 (0.0000627, 0.0001994)	0.0003367 (0.0001616, 0.0006970)

Exposure Route	Clothing	Data Set	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
		Experienced	0.0001081 (0.0000616, 0.0002000)	0.0003324 (0.0001539, 0.0007009)
Respirable 8-hr TWA (mg/m^3/lb AI)		All	0.0000157 (0.0000088, 0.0000293)	0.0000504 (0.0000238, 0.0001056)
		Exc. ME 17	0.0000136 (0.0000078, 0.0000249)	0.0000421 (0.0000202, 0.0000871)
		Experienced	0.0000135 (0.0000077, 0.0000250)	0.0000415 (0.0000192, 0.0000876)

Table 17. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Occupational Granules

Exposure Route	Clothing	Data Set	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	All	0.049 (0.035, 0.069)	0.118 (0.073, 0.188)
	Short Dermal	All	0.626 (0.422, 0.950)	1.645 (0.948, 2.818)
	Long Short Dermal	All	0.481 (0.280, 0.856)	1.499 (0.736, 3.002)
	Hands Only	All	0.014 (0.009, 0.023)	0.039 (0.022, 0.070)
Inhalation Concentration (mg/m^3/lb AI)		All	0.721 (0.426, 1.268)	2.223 (1.106, 4.396)
Inhalation Dose (mg/lb AI)		All	0.07843 (0.04358, 0.14815)	0.25500 (0.11934, 0.53545)
Inhalation 8-hr TWA (mg/m^3/lb AI)		All	0.00980 (0.00545, 0.01852)	0.03187 (0.01492, 0.06693)
Respirable Concentration (mg/m^3/lb AI)		All	0.02841 (0.01743, 0.04801)	0.08425 (0.04359, 0.16036)
Respirable Dose (mg/lb AI)		All	0.0032832 (0.0018038, 0.0060957)	0.0105066 (0.0049299, 0.0220069)
Respirable 8-hr TWA (mg/m^3/lb AI)		All	0.0004048 (0.0002255, 0.0007620)	0.0013133, (0.0006162, 0.0027509)

Table 18. Arithmetic mean and 95th percentile estimates from lognormal simple random sampling model for normalized exposure for Occupational Powder

Exposure Route	Clothing	Data Set	Arithmetic Mean (95% Confidence Interval)	95th Percentile (95% Confidence Interval)
Dermal (mg/lb AI)	Long Dermal	All	0.226 (0.145, 0.363)	0.631 (0.342, 1.157)
	Short Dermal	All	3.319 (2.031, 5.634)	9.786 (5.041, 18.884)
	Long Short Dermal	All	2.748 (1.434, 5.650)	9.298 (4.079, 21.038)
	Hands Only	All	0.078 (0.037, 0.183)	0.281 (0.111, 0.702)
Inhalation Concentration (mg/m^3/lb AI)		All	1.481 (0.947, 2.386)	4.149 (2.244, 7.628)
Inhalation Dose (mg/lb AI)		All	0.22432 (0.12829, 0.41304)	0.70770 (0.33923, 1.46672)
Inhalation 8-hr TWA (mg/m^3/lb AI)		All	0.02804 (0.01604, 0.05163)	0.08846 (0.04240, 0.18334)
Respirable Concentration (mg/m^3/lb AI)		All	0.01115 (0.00697, 0.01844)	0.03207 (0.01692, 0.06046)
Respirable Dose (mg/lb AI)		All	0.0017769 (0.0009586, 0.0035128)	0.0058727, 0.0026599, 0.0128744)
Respirable 8-hr TWA (mg/m^3/lb AI)		All	0.0002221 (0.0001198, 0.0004391)	0.0007341 (0.0003325, 0.0016093)

For each scenario, exposure route and data subset, the two statistical models were fitted to the observed data and the summary statistics listed above were calculated together with 95% confidence intervals. The 95% confidence intervals in Tables 15 to 18 were computed using a parametric bootstrap. For these calculations, the parametric bootstrap simulations were all generated from the fitted lognormal simple random sampling model, even for the empirical summary statistics, on the basis that the lognormal simple random sampling model is the best choice for modeling the data, even if the summary statistics are developed from a simpler statistical model. For example, in the "All" columns from Tables 1 to 10 and in all the columns from Tables 11 to 14, the empirical arithmetic means are presented, which are the arithmetic means of the 18 measurements. To estimate the uncertainty of those empirical arithmetic means, data are simulated from the lognormal simple random sampling model to calculate the parametric bootstrap confidence intervals. The arithmetic means in Tables 15 to 18 are estimated using the lognormal simple random sampling model, which is also used to estimate the confidence intervals in Tables 15 to 18. The unit exposure estimates (from the lognormal simple random sampling model) displayed in Tables 15 to 18 are recommended over the empirical arithmetic means and 95th percentiles displayed in Tables 1 to 14.

The algorithm used was as follows:

Step 1:

Assume that there are N subjects in a data subset. (N = 18 for the "All" subsets.)
Simulate N random variables Y, X from the estimated lognormal distribution superimposed upon the observed sampling structure ---;

Y = LnGM + RanNor(Seed)×Sr

X = exp(Y)

where:

LnGM = natural logarithm of fitted geometric mean

Sr = natural logarithm of fitted geometric standard deviation

Step 2:
For Y:

Calculate GMs = exp(EAM)

Calculate GSDs = exp(Su)

Calculate AMu = GMs×exp(0.5×Su×Su)

Calculate P95u = GMs× exp(Z95×Su)

where:

EAM = sample arithmetic mean of Y = AMu

Su = standard deviation of Y

For X:

Calculate arithmetic mean AMs

Calculate 95th percentile P95s

Step 3: Repeat Steps 1 and 2 10,000 times.

Steps 1 to 3 result in 10,000 values each for each of GSDs, GMs, AMs, AMu, P95s, and P95u. 95% confidence intervals can be defined for each parameter by the 2.5th and 97.5th percentiles (lower and upper, respectively) of the bootstrap distribution of that corresponding parameter. Note that by definition, GSDs = GSDu and GMs = GMu.

Similarly to Tables 1 to 14, the results for Consumer Granules and Consumer Powder show that excluding the outlier subject ME 9 for Consumer Granules and ME 17 for Consumer Powder reduced the arithmetic mean and 95th percentile, and also produced much narrower confidence intervals. Excluding the other two subjects without experience in using pool granular or powder chemicals had very little impact after the first subject was excluded.

4. Non-detects

For all the analyses presented in this memorandum except for Table 19, Table 20, Table 37, and Table 38, measurements below the LOQ were replaced by one half of the LOQ. In Table 19 and Table 20, we investigated the impact on the summary statistics of the exposure values below the LOQ, i.e., censored values. All the hand wash measurements in the study were above the LOQ of 10 µg. All but one of the face/neck wipes were above the LOQ of 10 µg; the exception was for ME5 of Consumer Granules. For the Consumer Granules, 6 of the inner dosimeter measurements and none of the outer dosimeter measurements were below the LOQ of 3 µg. For the other scenarios, all the inner and outer dosimeters were above the LOQ. For the inhalation exposure metrics, none of the PUF plug values were below the LOQ of 0.01 µg, three of the glass fiber filter values for Consumer Granules were below the LOQ of 0.01 µg, two of the glass fiber filter values for Consumer Powder were below the LOQ of 0.01 µg, and none of the glass fiber filter values were below the LOQ for Occupational Granules or Powder.

For each exposure metric, we computed the arithmetic mean and 95th percentiles using the recommended substitution of one half the LOQ for values below the LOQ and compared those results to estimates using the alternative substitutions of the LOQ (the maximum possible exposure estimate) and of zero (the minimum possible estimate). As an exception, we did not consider substitution of zero for the three respirable inhalation exposure metrics, because the statistical models use the logarithms of the exposure which cannot be calculated when the minimum exposure is zero. We did consider the substitution of zero for the inhalation exposure metrics computed from the sum of the glass fiber filter and PUF plug residues, since none of the PUF plug residues were zero, so the minimum inhalation concentration is non-zero.

We also investigated a censored maximum likelihood statistical method described in the following paragraph.

The lognormal simple random sampling model assumes that the exposure values are independent and identically lognormally distributed. For uncensored values with a mass m, the mass is between a lower bound of m and an upper bound of m. For censored mass values, the mass value is known to be between a lower bound and an upper bound. The lower bound for the mass is the sum of all the measured residue values after replacing any censored residues by zero (e.g., for any censored inner dosimeter or face/neck wipe measurement). The upper bound for the mass is the sum of all the measured residue values after replacing any censored residues by the LOQ (e.g., for any censored inner dosimeter or face/neck wipe measurement). For the six inhalation exposure metrics, the concentration, dose, or time-weighted average lower and upper bounds are each calculated using the lower and upper bounds for the mass together with the measured air volume and assumed breathing rate. The SAS procedure LIFEREG was used to fit the lognormal model to the combined censored and uncensored data using the maximum likelihood method. The procedure produces estimates of the geometric mean and geometric standard deviation for the fitted lognormal distribution.

To calculate confidence intervals for the arithmetic means and 95th percentiles, a parametric bootstrap method was used. This is exactly the same bootstrap method that was used for the original case where the non-detects were replaced by half the LOQ. 10,000 values of the unit exposure were simulated from the fitted lognormal distribution, and for each simulation, the geometric mean and geometric standard deviation were calculated and used to calculate the arithmetic mean (AMu) and 95th percentile (P95u) of the corresponding lognormal distribution. The simulated unit exposures are all uncensored numerical values even though the corresponding residues can be lower than the LOQs. The confidence intervals for the AMu and P95u range from the 2.5th percentile to the 97.5th percentile.

Results for the Short Dermal and Inhalation Concentration exposure metrics for Consumer Granules are presented in Table 19. Results for the Inhalation Concentration exposure metrics for Consumer Powders are presented in Table 20. Results for the other exposure metrics are not presented here to avoid a voluminous memorandum but can be provided upon request or obtained by running the provided SAS program. There were no non-detects for dermal exposure for Consumer Powders or for the two occupational scenarios. The results are compared for the default substitution of half the LOQ, the alternative substitutions of the LOQ and zero, and estimates calculated using the maximum likelihood method for censored data, referred to as “Censored data MLE.”

Table 19. Exposure summary statistics for Consumer Granules calculated using alternative estimated exposures for values below the LOQ

Exposure Route	Clothing	Data Set	Method for Substituting Values Below the LOQ	Arithmetic Mean	95th Percentile
Dermal (mg/lb AI)	Short Dermal	All	Substitute ½ LOQ	1.874 (0.624, 6.668)	7.248 (2.196, 23.179)
			Substitute LOQ	1.872 (0.624, 6.647)	7.241 (2.196, 23.132)
			Substitute Zero	1.876 (0.624, 6.691)	7.255 (2.195, 23.230)
			Censored data MLE	1.739 (0.606, 5.868)	6.718 (2.105, 20.794)
		Exc. ME 9	Substitute ½ LOQ	0.948 (0.412, 2.422)	3.499 (1.293, 9.219)
			Substitute LOQ	0.948 (0.412, 2.417)	3.495 (1.293, 9.198)
			Substitute Zero	0.949 (0.411, 2.430)	3.503 (1.293, 9.242)
			Censored data MLE	0.899 (0.403, 2.202)	3.276 (1.247, 8.387)
		Experienced	Substitute ½ LOQ	1.038 (0.394, 3.138)	3.918 (1.266, 11.812)
			Substitute LOQ	1.037 (0.394, 3.130)	3.914 (1.266, 11.785)
			Substitute Zero	1.038 (0.393, 3.145)	3.921 (1.265, 11.842)
			Censored data MLE	0.970 (0.386, 2.762)	3.618 (1.214, 10.509)
Inhalation concentration ((mg/m^3)/lb AI)		All	Substitute ½ LOQ	0.043 (0.026, 0.074)	0.130 (0.065, 0.252)
			Substitute LOQ	0.043 (0.026, 0.074)	0.131 (0.066, 0.255)
			Substitute Zero	0.043 (0.026, 0.073)	0.129 (0.065, 0.250)
			Censored data MLE	0.042 (0.026, 0.070)	0.124 (0.064, 0.237)
		Exc. ME 9	Substitute ½ LOQ	0.041 (0.024, 0.070)	0.122 (0.061, 0.241)
			Substitute LOQ	0.041 (0.024, 0.071)	0.123 (0.061, 0.243)
			Substitute Zero	0.040 (0.024, 0.070)	0.121 (0.060, 0.238)
			Censored data MLE	0.040 (0.024, 0.067)	0.117 (0.059, 0.225)
		Experienced	Substitute ½ LOQ	0.044 (0.025, 0.084)	0.138 (0.063, 0.294)
			Substitute LOQ	0.045 (0.025, 0.084)	0.139 (0.064, 0.298)
			Substitute Zero	0.044 (0.025, 0.083)	0.136 (0.063, 0.291)
			Censored data MLE	0.043 (0.024, 0.078)	0.130 (0.061, 0.271)

Table 20. Exposure summary statistics for Consumer Powder calculated using alternative estimated exposures for values below the LOQ

Exposure Route	Clothing	Data Set	Method for Substituting Values Below the LOQ	Arithmetic Mean	95th Percentile
Inhalation concentration ((mg/m^3)/lb AI)		All	Substitute ½ LOQ	1.190 (0.526, 2.927)	4.360 (1.673, 11.209)
			Substitute LOQ	1.191 (0.526, 2.929)	4.363 (1.675, 11.217)
			Substitute Zero	1.189 (0.525, 2.925)	4.357 (1.672, 11.201)
			Censored data MLE	1.134 (0.517, 2.694)	4.102 (1.617, 10.269)
		Exc. ME 9	Substitute ½ LOQ	0.912 (0.440, 2.091)	3.216 (1.295, 7.921)
			Substitute LOQ	0.913 (0.440, 2.093)	3.219 (1.296, 7.929)
			Substitute Zero	0.912 (0.439, 2.089)	3.213 (1.294, 7.913)
			Censored data MLE	0.874 (0.433, 1.929)	3.030 (1.254, 7.264)
		Experienced	Substitute ½ LOQ	1.064 (0.494, 2.523)	3.760 (1.424, 9.636)
			Substitute LOQ	1.065 (0.494, 2.525)	3.763 (1.425, 9.643)
			Substitute Zero	1.063 (0.493, 2.521)	3.757 (1.423, 9.628)
			Censored data MLE	1.013 (0.488, 2.296)	3.513 (1.375, 8.719)

The results in Tables 19 and 20 show very small impacts of the alternative substitution approaches for treating values below the LOQ on the unit exposure arithmetic mean and 95th percentile, which is due to the small number of non-detect values. The censored data MLE statistics are lower than the values for the substitution method, but that is easily explained by the fact that the maximum likelihood method tends to underestimate standard deviations compared to the restricted maximum likelihood method used for sample statistics. In particular, for uncensored data, the maximum likelihood method uses n as the divisor for calculating the variance but the restricted maximum likelihood method uses n − 1 as the divisor for the variance.

5. Fold Relative Accuracy

Fold relative accuracy (*fRA*) is a measure that can be used to determine how well a statistic can describe its population parameter. Let us assume θ is a parameter and T is the sample statistic of θ (i.e., an estimate of θ). If the 2.5th and 97.5th percentiles of the sampling distribution of T can be denoted by $T_{2.5}$ and $T_{97.5}$, respectively, then the 95th percentile of sample fold relative accuracy can be theoretically calculated using the following formula provided in the AHETF Governing Document (AHETF, 2007, pg. 136 and AHETF, 2011, pg. 120):

$$fRA_{95} = \text{Max}\,(T_{97.5} / \theta, \theta / T_{2.5})$$

The actual value of θ is unknown. Thus, fRA_{95} was calculated by substituting θ with T. If the fRA_{95} of a statistic were equal to 3, then it would be correct to say: "At least 95% of the time the sample statistic will be accurate to within 3-fold of the population value". According to the AHETF Governing Document, the statistical design of the exposure

monitoring study should be adequate to produce a fRA_{95} less than or equal to 3. Thus the confidence intervals calculated in the above algorithm can be used to estimate the fold relative accuracy and compare the observed fRA with the study design benchmark of 3. If the observed fold relative accuracy is greater than 3, this means that the experiment did not meet the benchmark, which would be due to differences between the distributions of the data used to design the study and the experimental data collected in the study. If the fold relative accuracy benchmark is not met, then it might be desirable to collect more data for this scenario in order to meet the benchmark.

Following HSRB recommendations, confidence intervals were estimated using both a parametric bootstrap approach, as described above, and the following non-parametric bootstrap approach. The non-parametric bootstrap method should be more robust since it does not assume that the fitted parametric model is the correct one. For the non-parametric bootstrap, exactly the same algorithm was used except that Step 1 above was replaced by the following:

Step 1:
Simulate N random variables Y, X by resampling at random with replacement from the original data:

The original exposure data are X(1), X(2), …, X(N), where N is the number of subjects in the data set.
Sample N values at random with replacement from the exposure values X(1), X(2), …, X(N). This gives the N simulated random variables X.
Y = log(X).

6. Detailed Summary Statistics with Confidence Intervals and Fold Relative Accuracy

Table 21 to Table 36 present the estimates, parametric and non-parametric confidence intervals and fold relative accuracy values for all the summary statistics for the various data subsets, for Short Dermal for the two Consumer scenarios, for Long Dermal for the two Occupational scenarios, and for Inhalation Concentration for all four scenarios. To avoid a voluminous memorandum, results for the other exposures routes are not presented here but can be made available upon request.

Table 21. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Short Dermal exposure (mg/lb AI) for Consumer Granules using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	5.143	2.965	8.939	1.74	2.176	8.816	2.36
GMs	0.490	0.235	1.058	2.16	0.250	1.063	2.17
AMs	2.937	0.549	5.484	5.35	0.360	6.839	8.15
AMu	1.874	0.624	6.668	3.56	0.382	9.877	5.27
P95s	26.788	2.159	64.758	12.41	0.928	26.788	28.86
P95u	7.248	2.196	23.179	3.30	1.056	33.518	6.87

Table 22. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Short Dermal exposure (mg/lb AI) for Consumer Powder using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	3.551	2.331	5.438	1.53	2.165	5.090	1.64
GMs	4.299	2.410	7.726	1.80	2.478	7.650	1.78
AMs	10.494	4.155	20.683	2.53	3.687	20.524	2.85
AMu	9.595	4.414	22.537	2.35	3.934	23.317	2.44
P95s	80.527	13.055	189.913	6.17	8.434	80.527	9.55
P95u	34.557	13.733	85.849	2.52	11.108	89.108	3.11

Table 23. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Long Dermal exposure (mg/lb AI) for Occupational Granules using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	1.946	1.562	2.425	1.25	1.537	2.322	1.27
GMs	0.039	0.029	0.054	1.36	0.029	0.053	1.34
AMs	0.048	0.035	0.069	1.44	0.035	0.062	1.35
AMu	0.049	0.035	0.069	1.41	0.036	0.064	1.36
P95s	0.128	0.072	0.286	2.24	0.071	0.128	1.81
P95u	0.118	0.073	0.188	1.61	0.076	0.164	1.56

Table 24. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Long Dermal exposure (mg/lb AI) for Occupational Powder using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	2.310	1.750	3.061	1.33	1.748	2.682	1.32
GMs	0.159	0.109	0.235	1.47	0.108	0.231	1.47
AMs	0.207	0.142	0.352	1.70	0.151	0.264	1.37
AMu	0.226	0.145	0.363	1.61	0.158	0.285	1.43
P95s	0.409	0.336	1.979	4.84	0.316	0.409	1.29

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
P95u	0.631	0.342	1.157	1.84	0.430	0.785	1.47

Table 25. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Short Dermal exposure (mg/lb AI) for Consumer Granules using All data excluding ME 9

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	3.811	2.407	6.010	1.58	1.927	6.788	1.98
GMs	0.387	0.205	0.734	1.89	0.218	0.751	1.94
AMs	1.534	0.379	2.207	4.05	0.309	3.827	4.96
AMu	0.948	0.412	2.422	2.56	0.323	3.695	3.90
P95s	19.277	1.238	20.577	15.57	0.732	19.277	26.35
P95u	3.499	1.293	9.219	2.71	0.864	13.896	4.05

Table 26. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Short Dermal exposure (mg/lb AI) for Consumer Powder using All data excluding ME 17

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	3.224	2.155	4.800	1.50	2.002	4.852	1.61
GMs	3.766	2.143	6.611	1.76	2.225	6.601	1.75
AMs	8.706	3.524	15.112	2.47	3.206	18.261	2.72
AMu	7.471	3.718	16.370	2.19	3.361	18.337	2.45
P95s	80.527	10.403	118.744	7.74	7.176	80.527	11.22
P95u	25.824	10.743	61.591	2.40	9.433	70.172	2.74

Table 27. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Short Dermal exposure (mg/lb AI) for Consumer Granules using data from experienced consumers only

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	4.157	2.452	6.955	1.70	1.972	7.482	2.11
GMs	0.376	0.185	0.792	2.11	0.198	0.794	2.11

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
AMs	1.673	0.360	2.658	4.64	0.290	4.262	5.77
AMu	1.038	0.394	3.138	3.02	0.299	4.672	4.50
P95s	19.277	1.161	24.338	16.61	0.732	19.277	26.35
P95u	3.918	1.266	11.812	3.10	0.797	17.126	4.91

Table 28. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Short Dermal exposure (mg/lb AI) for Consumer Powder using data from experienced consumers only

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	3.216	2.091	4.924	1.54	1.878	5.003	1.71
GMs	4.032	2.263	7.237	1.79	2.308	7.229	1.79
AMs	9.383	3.632	16.592	2.58	3.233	20.058	2.90
AMu	7.977	3.877	17.873	2.24	3.382	20.923	2.62
P95s	80.527	9.937	127.319	8.10	7.176	80.527	11.22
P95u	27.544	10.866	67.849	2.53	9.140	80.260	3.01

Table 29. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Inhalation Concentration exposure ((mg/m^3)/lb AI) for Consumer Granules using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	2.557	1.865	3.510	1.37	1.932	3.181	1.32
GMs	0.028	0.018	0.043	1.55	0.018	0.042	1.53
AMs	0.040	0.025	0.072	1.79	0.026	0.056	1.54
AMu	0.043	0.026	0.074	1.72	0.027	0.063	1.62
P95s	0.122	0.065	0.455	3.73	0.071	0.122	1.71
P95u	0.130	0.065	0.252	1.98	0.069	0.200	1.87

Table 30. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Inhalation Concentration exposure ((mg/m³)/lb AI) for Consumer Powder using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	3.724	2.407	5.796	1.56	2.165	5.282	1.72
GMs	0.501	0.275	0.921	1.84	0.286	0.935	1.86
AMs	1.397	0.492	2.658	2.84	0.433	2.792	3.23
AMu	1.190	0.526	2.927	2.46	0.412	3.223	2.89
P95s	11.132	1.588	25.550	7.01	1.936	11.132	5.75
P95u	4.360	1.673	11.209	2.61	1.111	12.404	3.93

Table 31. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Inhalation Concentration exposure ((mg/m³)/lb AI) for Occupational Granules using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	2.638	1.916	3.636	1.38	1.764	3.590	1.50
GMs	0.451	0.288	0.708	1.57	0.290	0.685	1.55
AMs	0.671	0.413	1.236	1.84	0.418	1.003	1.60
AMu	0.721	0.426	1.268	1.76	0.452	1.117	1.59
P95s	2.849	1.079	8.140	2.86	0.800	2.849	3.56
P95u	2.223	1.106	4.396	2.01	1.114	3.783	2.00

Table 32. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Inhalation Concentration exposure ((mg/m³)/lb AI) for Occupational Powder using All data

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	2.319	1.755	3.077	1.33	1.931	2.555	1.20
GMs	1.040	0.710	1.535	1.48	0.704	1.535	1.48
AMs	1.398	0.929	2.312	1.65	0.962	1.856	1.45
AMu	1.481	0.947	2.386	1.61	0.952	2.009	1.56
P95s	2.889	2.205	13.076	4.53	2.342	2.889	1.23
P95u	4.149	2.244	7.628	1.85	2.485	5.464	1.67

Table 33. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Inhalation Concentration exposure ((mg/m³)/lb AI) for Consumer Granules using All data excluding ME 9

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	2.552	1.850	3.510	1.38	1.889	3.202	1.35
GMs	0.026	0.017	0.041	1.56	0.017	0.040	1.53
AMs	0.038	0.023	0.068	1.79	0.024	0.055	1.60
AMu	0.041	0.024	0.070	1.73	0.024	0.062	1.67
P95s	0.122	0.059	0.422	3.47	0.065	0.122	1.88
P95u	0.122	0.061	0.241	2.01	0.062	0.198	1.98

Table 34. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Inhalation Concentration exposure ((mg/m³)/lb AI) for Consumer Powder using All data excluding ME 17

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	3.366	2.216	5.087	1.52	1.932	5.088	1.74
GMs	0.437	0.243	0.783	1.79	0.261	0.803	1.84
AMs	1.172	0.414	1.910	2.83	0.351	2.552	3.34
AMu	0.912	0.440	2.091	2.29	0.340	2.608	2.86
P95s	11.132	1.253	15.646	8.89	1.027	11.132	10.84
P95u	3.216	1.295	7.921	2.48	0.835	10.043	3.85

Table 35. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Inhalation Concentration exposure ((mg/m³)/lb AI) for Consumer Granules using data from experienced consumers only

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	2.669	1.855	3.806	1.44	1.933	3.417	1.38
GMs	0.027	0.017	0.046	1.67	0.017	0.044	1.63
AMs	0.041	0.024	0.081	1.99	0.025	0.059	1.64
AMu	0.044	0.025	0.084	1.89	0.025	0.068	1.75
P95s	0.122	0.059	0.484	3.98	0.065	0.122	1.88
P95u	0.138	0.063	0.294	2.18	0.067	0.223	2.05

Table 36. Arithmetic mean, geometric mean, geometric standard deviation, and 95th percentiles (with 95% confidence intervals and fold relative accuracy), for different statistical models of the normalized Inhalation Concentration exposure ((mg/m³)/lb AI) for Consumer Powder using data from experienced consumers only

		Parametric Bootstrap			Non-parametric Bootstrap		
Parameter	Estimate	Lower Bound	Upper Bound	Fold Relative Accuracy	Lower Bound	Upper Bound	Fold Relative Accuracy
GSDs	3.385	2.160	5.281	1.57	1.897	5.177	1.78
GMs	0.506	0.277	0.932	1.84	0.291	0.941	1.86
AMs	1.309	0.461	2.321	2.84	0.389	2.826	3.36
AMu	1.064	0.494	2.523	2.37	0.383	3.073	2.89
P95s	11.132	1.297	18.587	8.58	1.027	11.132	10.84
P95u	3.760	1.424	9.636	2.64	0.925	11.737	4.06

Tables 21 to 28 show that the study benchmark design value of 3 for the fold relative accuracy was generally met for Short Dermal in the Consumer Powder scenario, and for Long Dermal in the Occupational Granules and Occupational Powder scenarios, except sometimes for the empirical 95th percentile P95s, which can have values up to about 11 for the fold relative accuracy. For Short Dermal in the Consumer Granules scenario, the study benchmark design value of 3 for the fold relative accuracy was generally not met for the arithmetic mean and 95th percentile, even after excluding ME 9 or the inexperienced consumers. Tables 29 to 36 show that for Inhalation Concentration the study benchmark design value of 3 for the fold relative accuracy was generally met for all scenarios and statistics except sometimes for the empirical 95th percentile P95s, which can have values up to about 10 for the fold relative accuracy. The data for the other dermal exposure routes (not shown here) follows the same pattern as shown for Long or Short Dermal. The data for the other inhalation exposure routes (not shown here) follows the same pattern as for Inhalation Concentration.

7. Empirical Quantile Plots

Quantile-quantile plots of the normalized exposure values were used to evaluate whether the data were lognormally distributed, as implied by the assumed statistical lognormal models. These plots were intended to help determine whether the data supported using untransformed normalized exposure values (exposure per pound AI) or log-transformed values or neither. The plots are not intended to evaluate the fitted regression models for the un-normalized exposure to be described in Section 9 below, for which the residual quantile plots were developed.

In each case the quantile-quantile plot compared the observed quantiles of the measured values with the corresponding quantiles of a normal or lognormal distribution. A perfect fit would imply that the plotted values lie in a straight line. For each data set, the quantile-quantile plots for the Short Dermal in the Consumer scenarios, the Long Dermal in the Occupational scenarios, and Inhalation Concentration exposure for all four scenarios are presented in Figure 1 to Figure 32. In most cases the plots show that the lognormal distribution is a better fit than the normal distribution for the normalized exposure. The quantile plots for the other exposure routes (not shown here) present similar patterns.

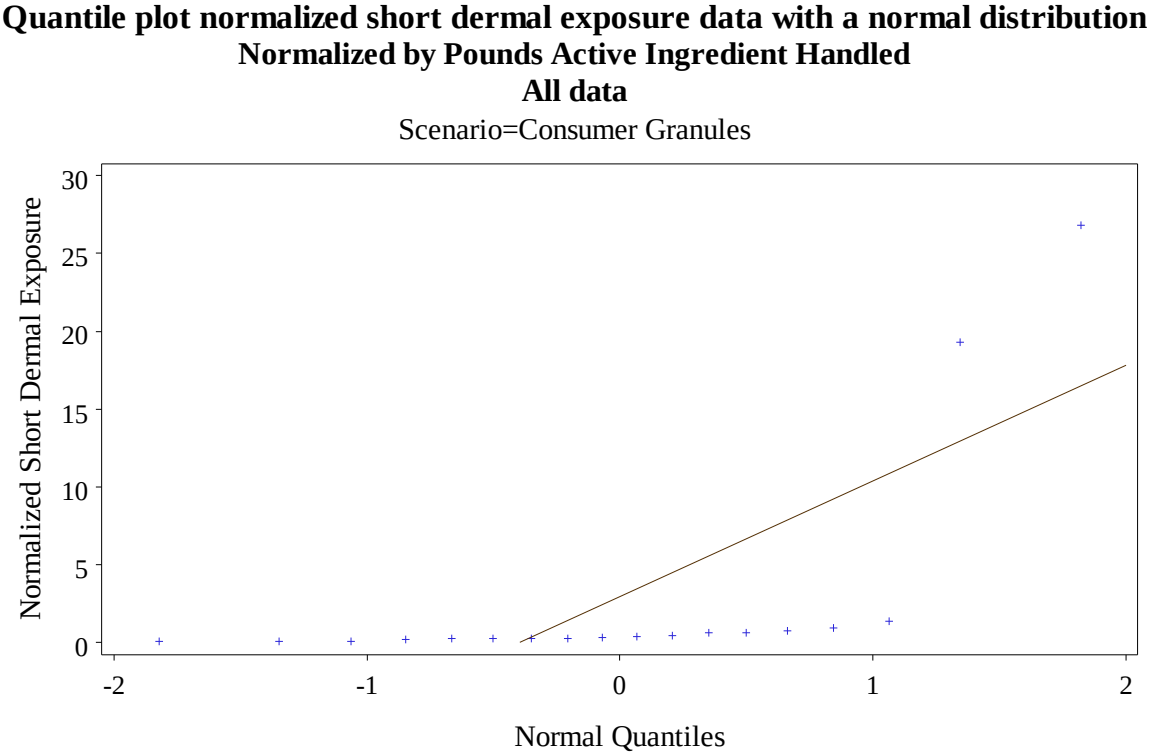

Figure 1. Empirical quantile plot for Short Dermal, Consumer Granules, All data, with a normal distribution

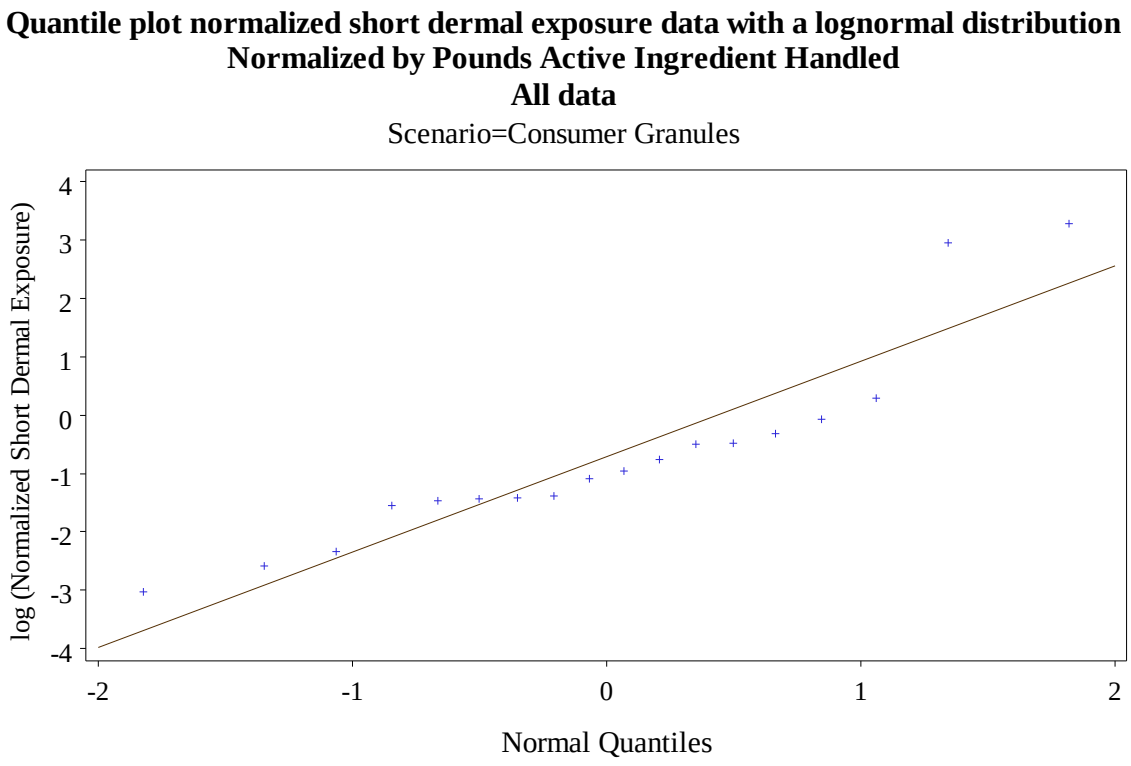

Figure 2. Empirical quantile plot for Short Dermal, Consumer Granules, All data, with a lognormal distribution

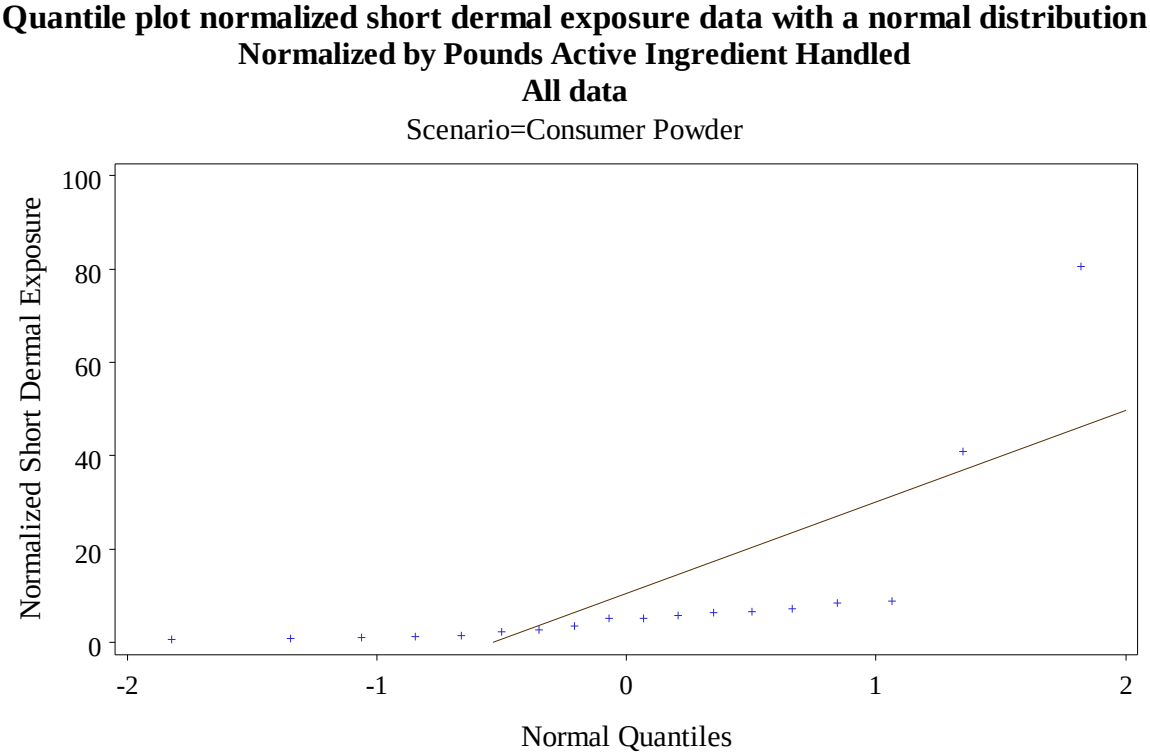

Figure 3. Empirical quantile plot for Short Dermal, Consumer Powder, All data, with a normal distribution

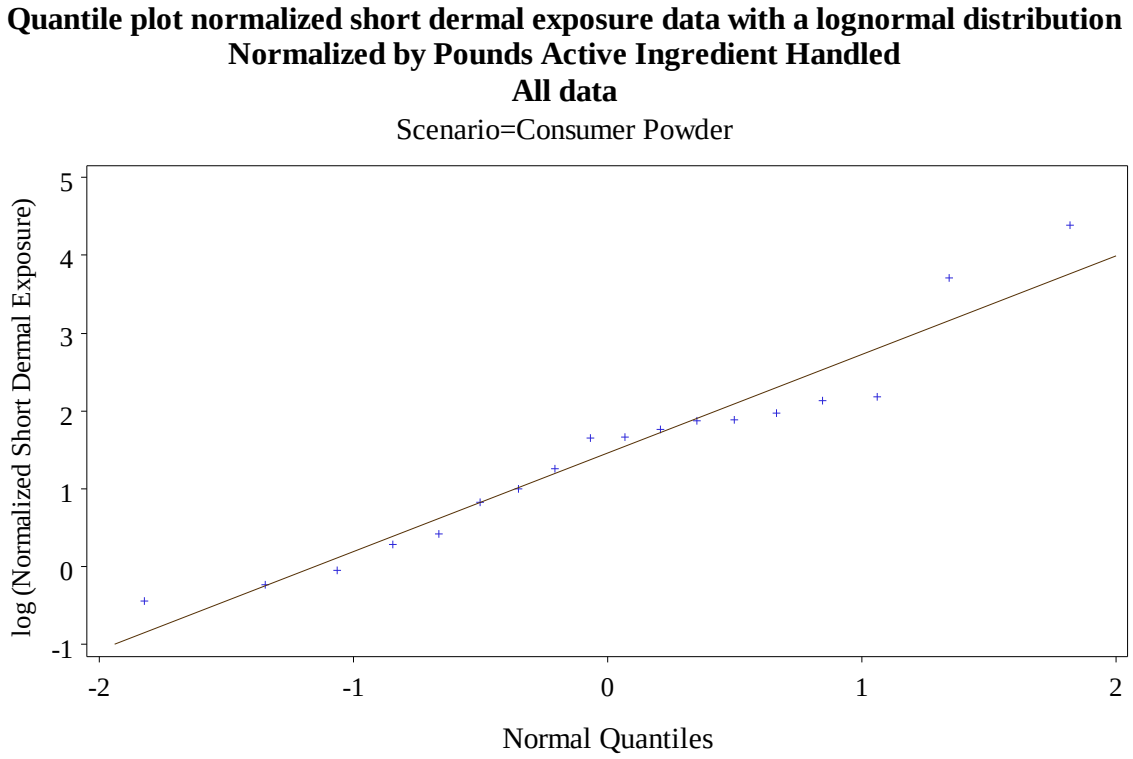

Figure 4. Empirical quantile plot for Short Dermal, Consumer Powder, All data, with a lognormal distribution

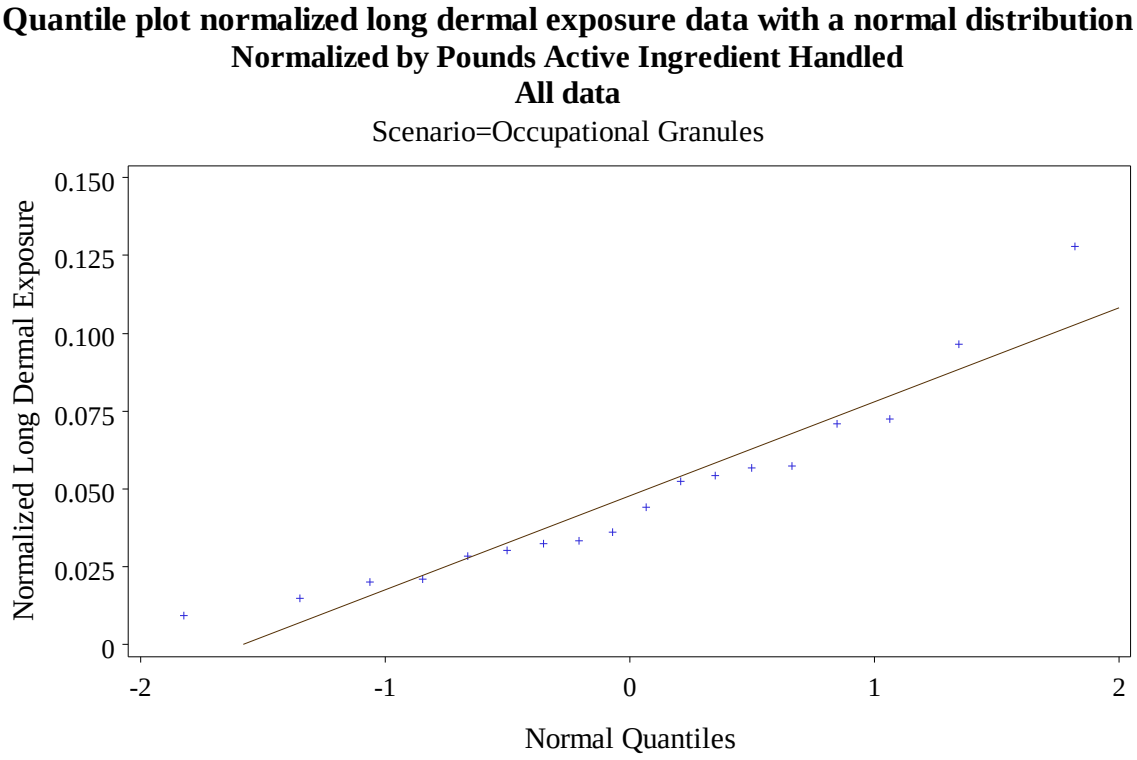

Figure 5. Empirical quantile plot for Long Dermal, Occupational Granules, All data, with a normal distribution

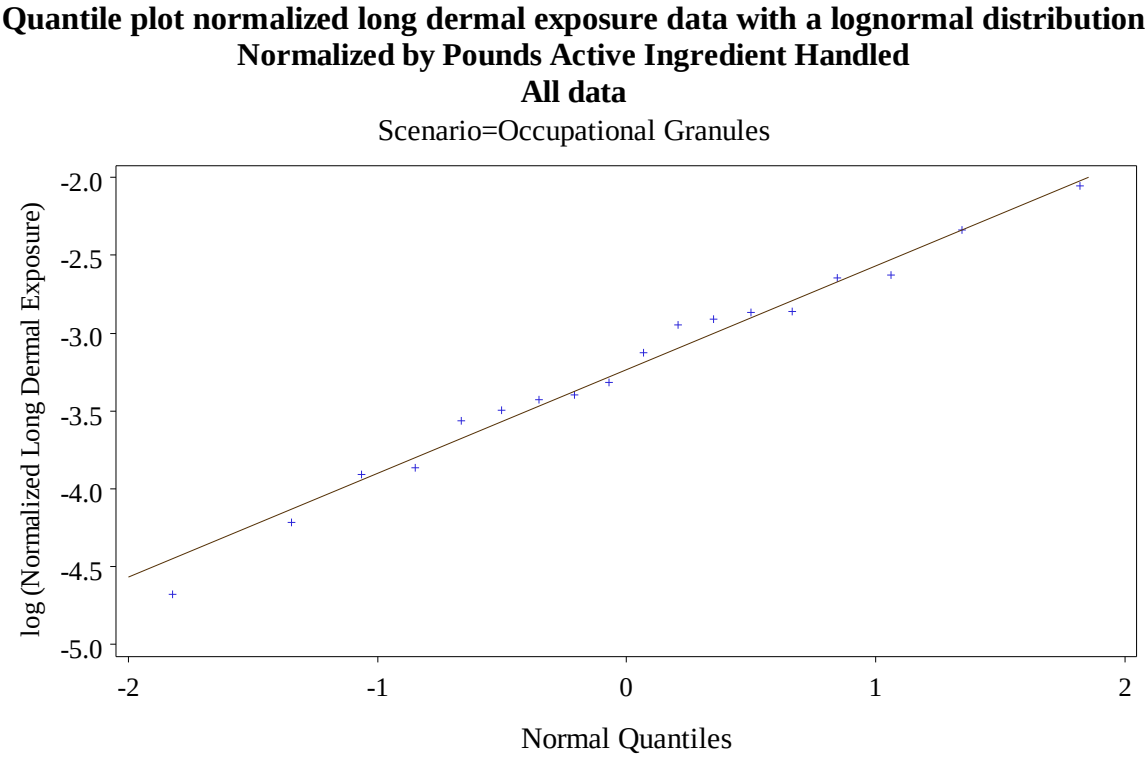

Figure 6. Empirical quantile plot for Long Dermal, Occupational Granules, All data, with a lognormal distribution

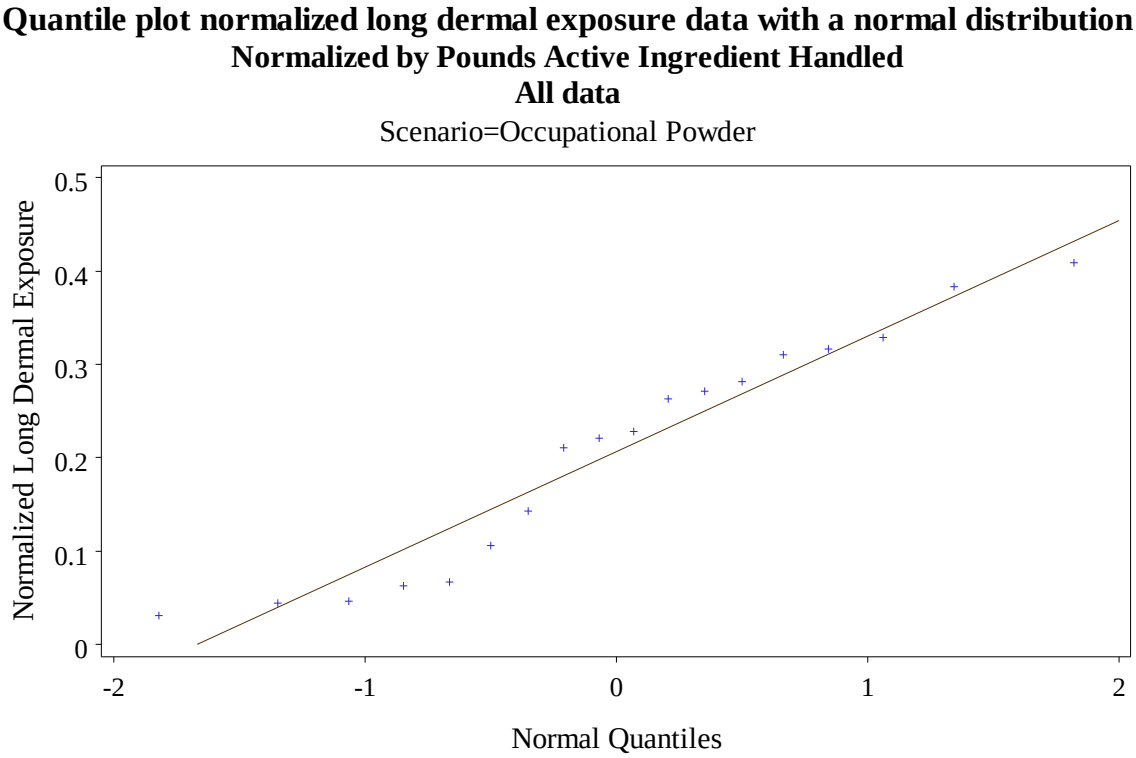

Figure 7. Empirical quantile plot for Long Dermal, Occupational Powder, All data, with a normal distribution

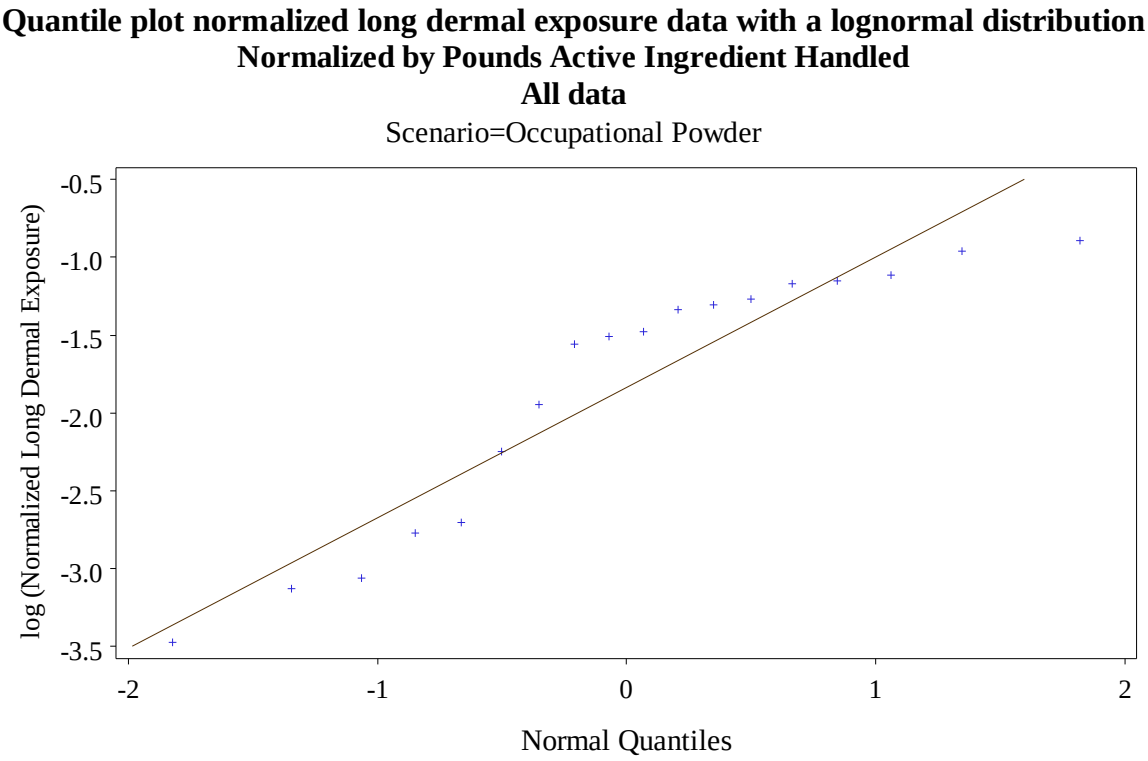

Figure 8. Empirical quantile plot for Long Dermal, Occupational Powder, All data, with a lognormal distribution

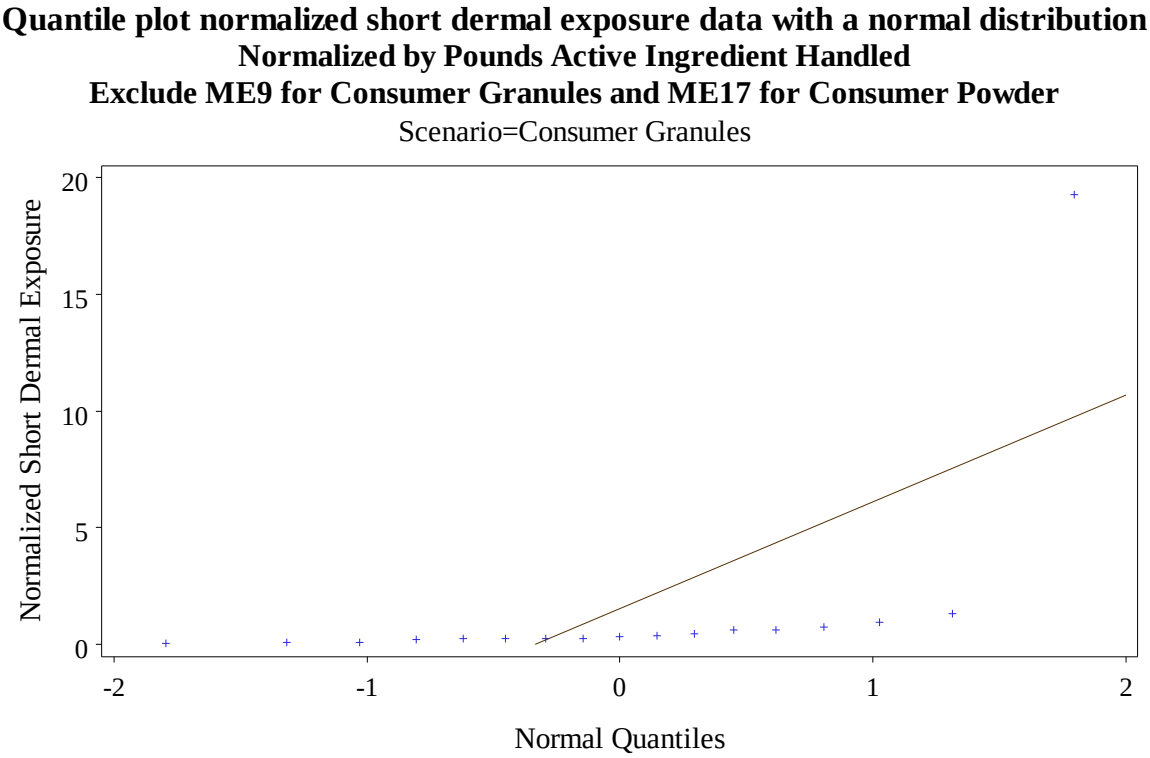

Figure 9. Empirical quantile plot for Short Dermal, Consumer Granules, Exc. ME 9, with a normal distribution

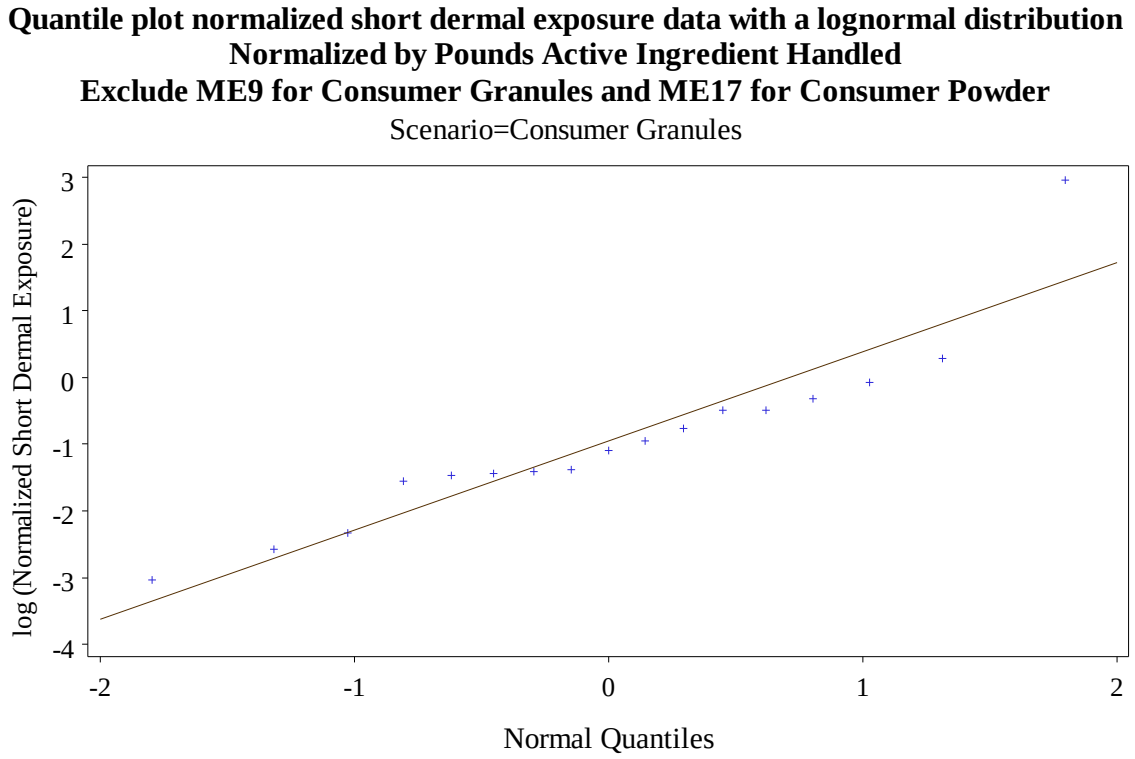

Figure 10. Empirical quantile plot for Short Dermal, Consumer Granules, Exc. ME 9, with a lognormal distribution

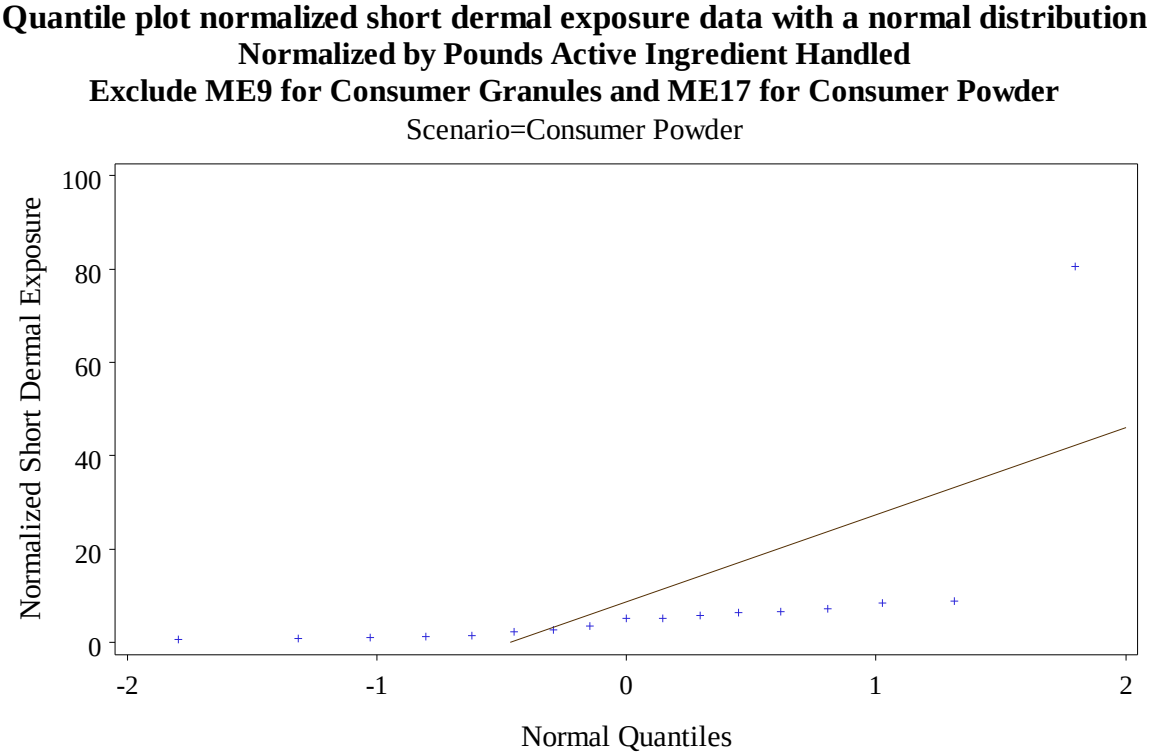

Figure 11. Empirical quantile plot for Short Dermal, Consumer Powder, Exc. ME 17, with a normal distribution

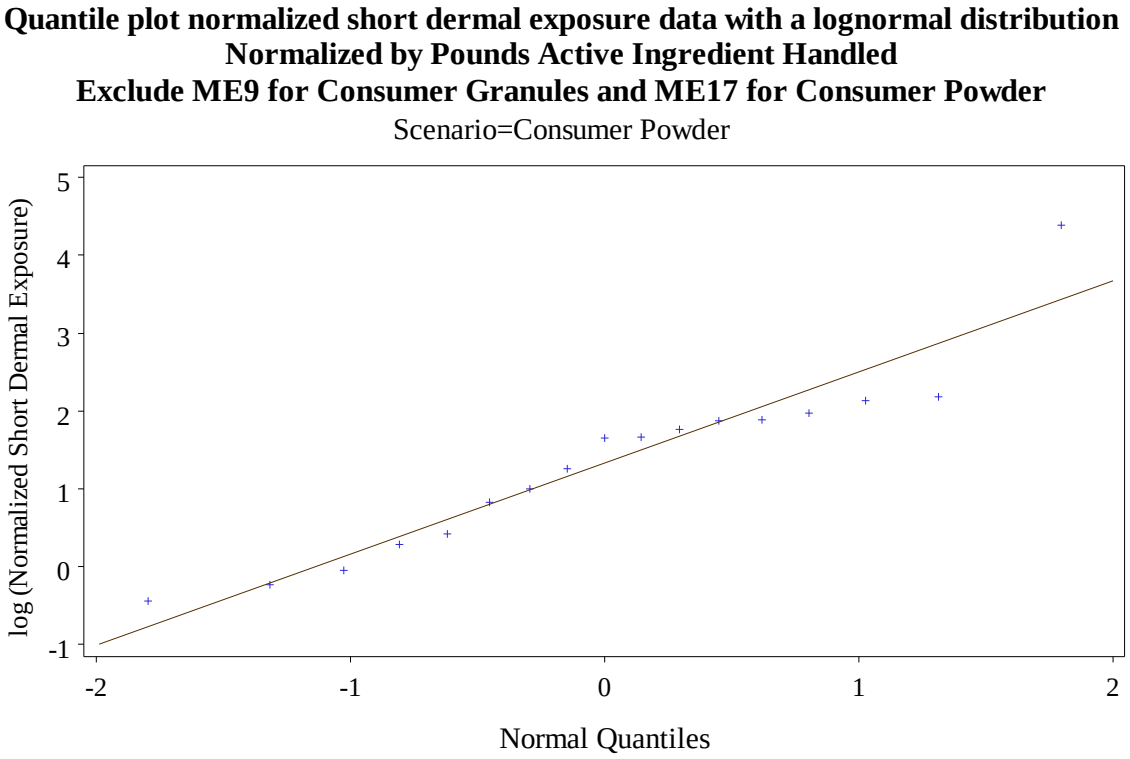

Figure 12. Empirical quantile plot for Short Dermal, Consumer Powder, Exc. ME 17, with a lognormal distribution

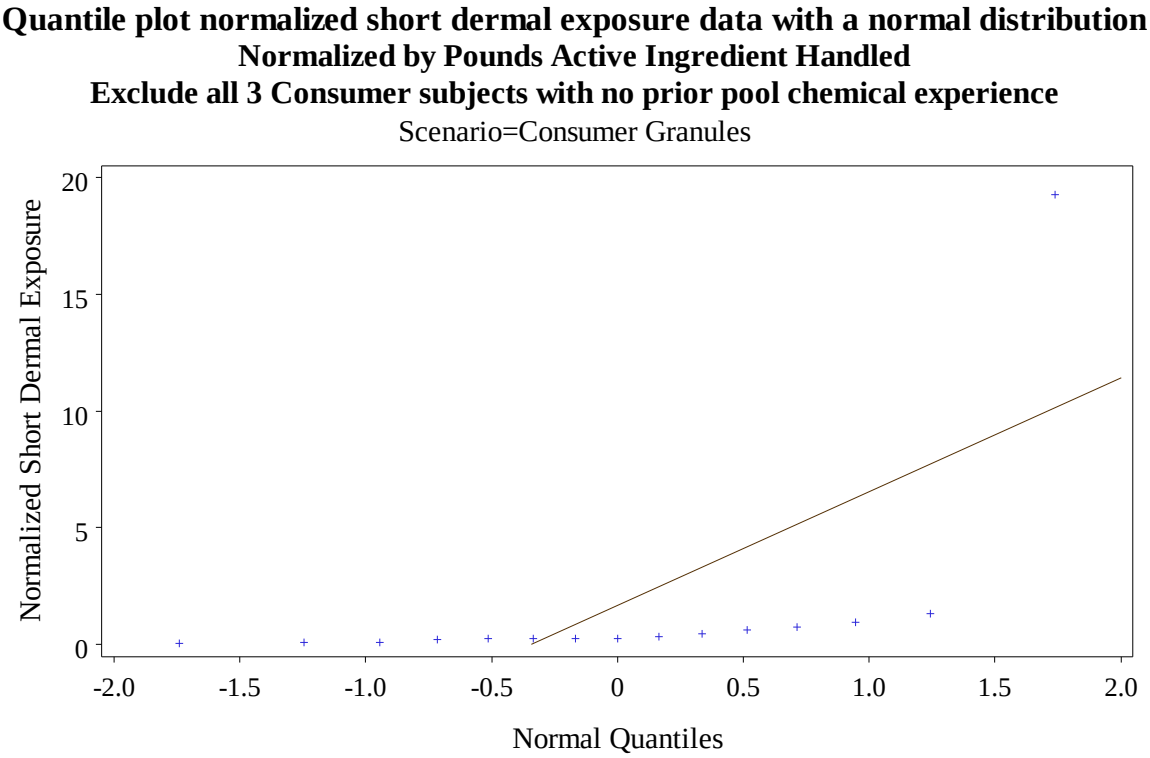

Figure 13. Empirical quantile plot for Short Dermal, Consumer Granules, Experienced consumers, with a normal distribution

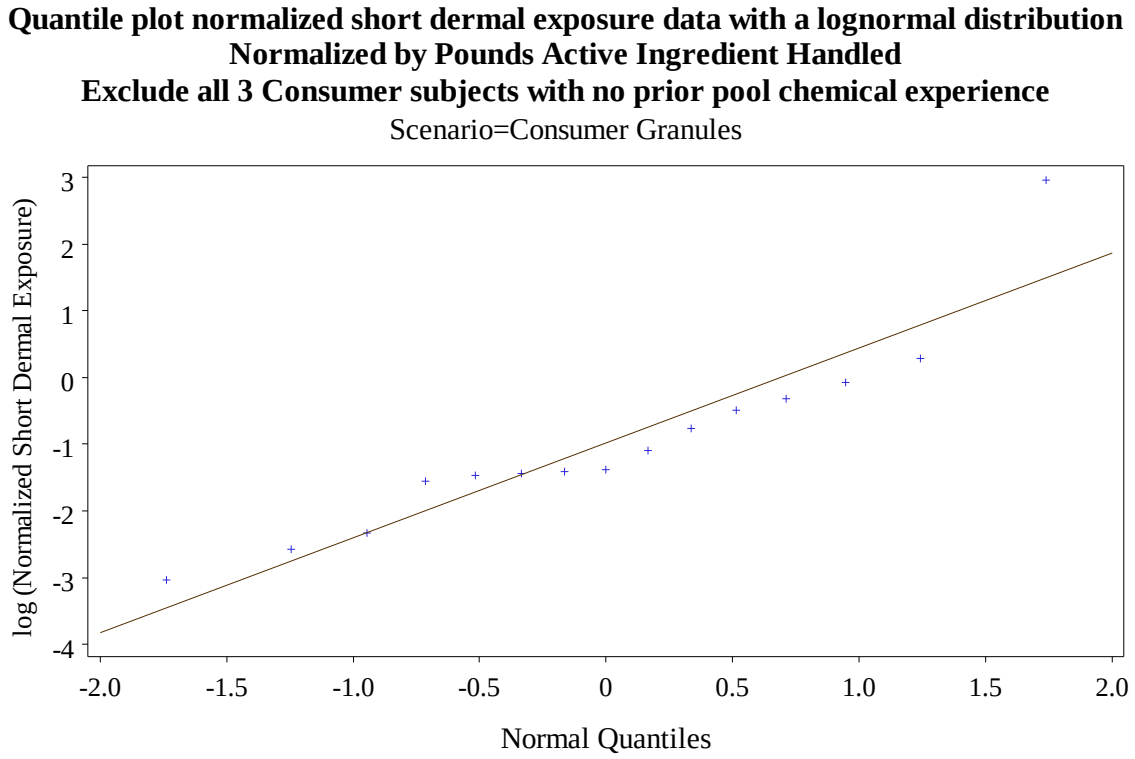

Figure 14. Empirical quantile plot for Short Dermal, Consumer Granules, Experienced consumers, with a lognormal distribution

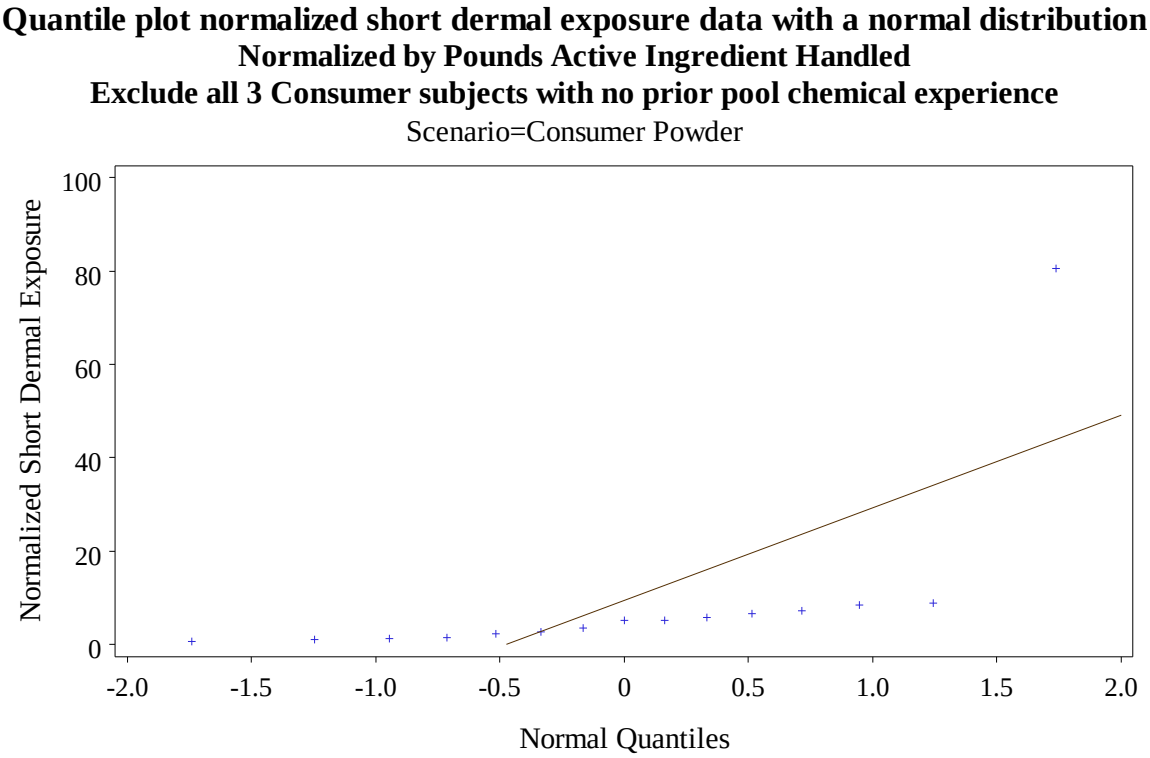

Figure 15. Empirical quantile plot for Short Dermal, Consumer Powder, Experienced consumers, with a normal distribution

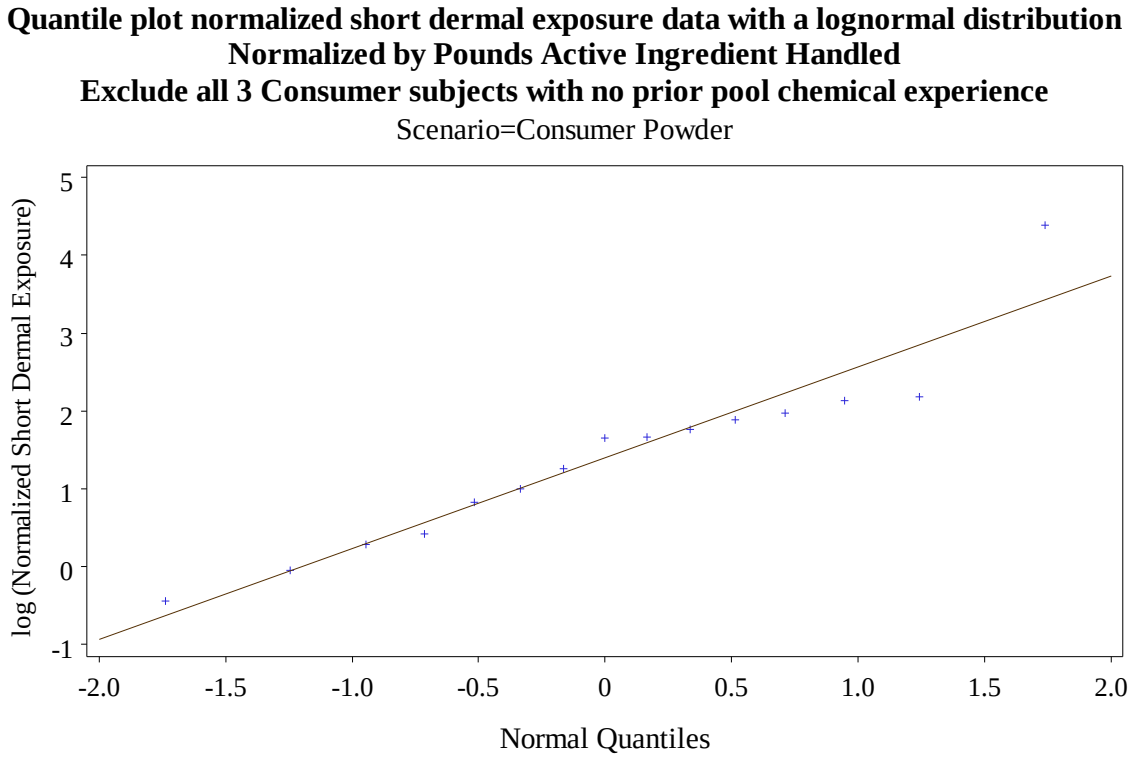

Figure 16. Empirical quantile plot for Short Dermal, Consumer Powder, Experienced consumers, with a lognormal distribution

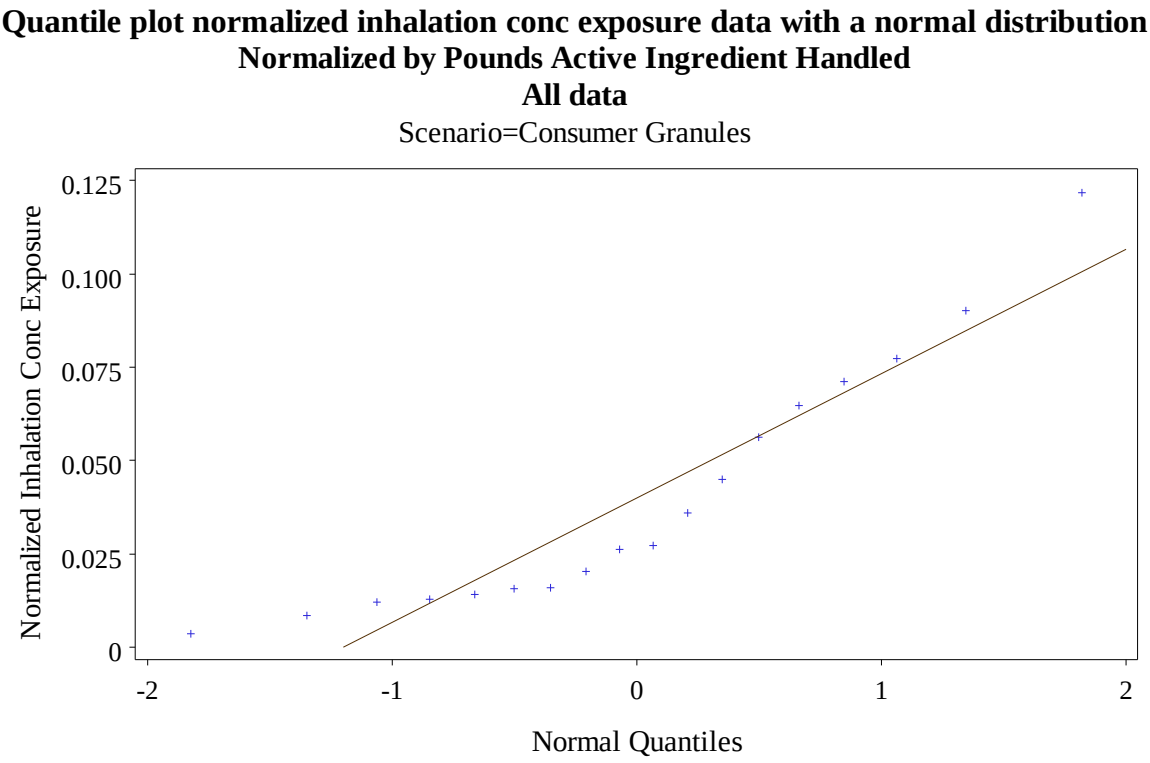

Figure 17. Empirical quantile plot for Inhalation Concentration, Consumer Granules, All data, with a normal distribution

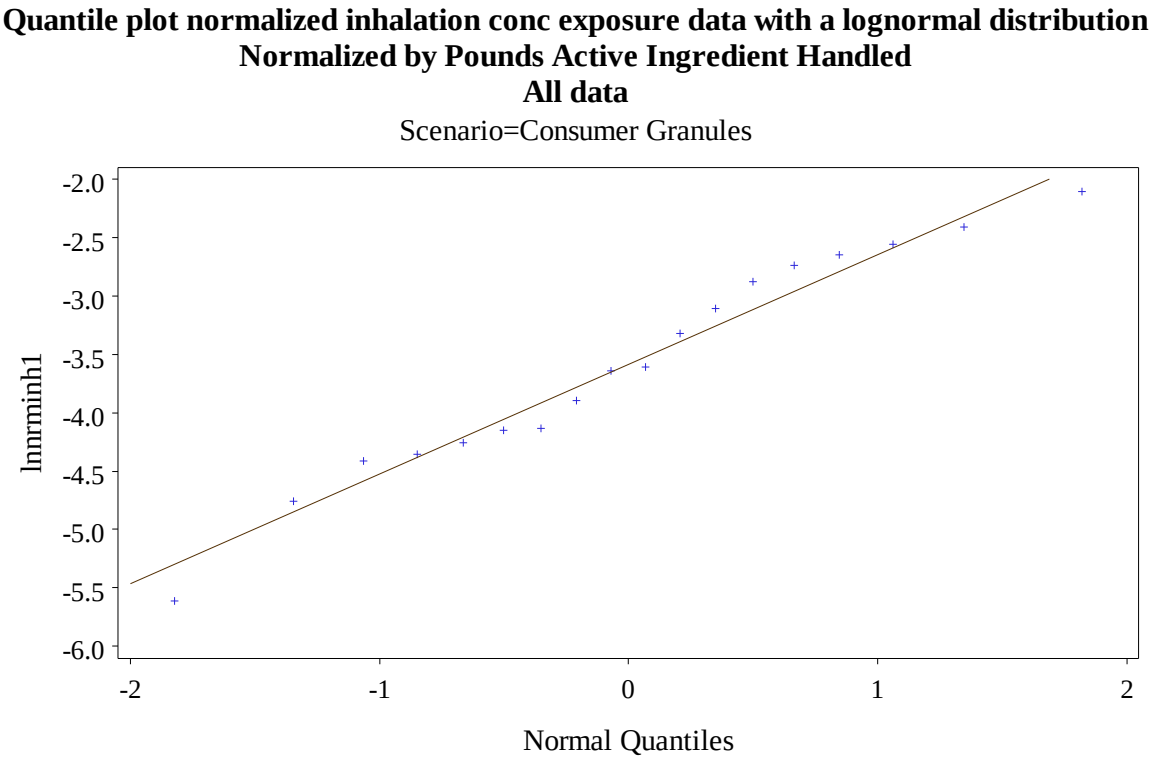

Figure 18. Empirical quantile plot for Inhalation Concentration, Consumer Granules, All data, with a lognormal distribution

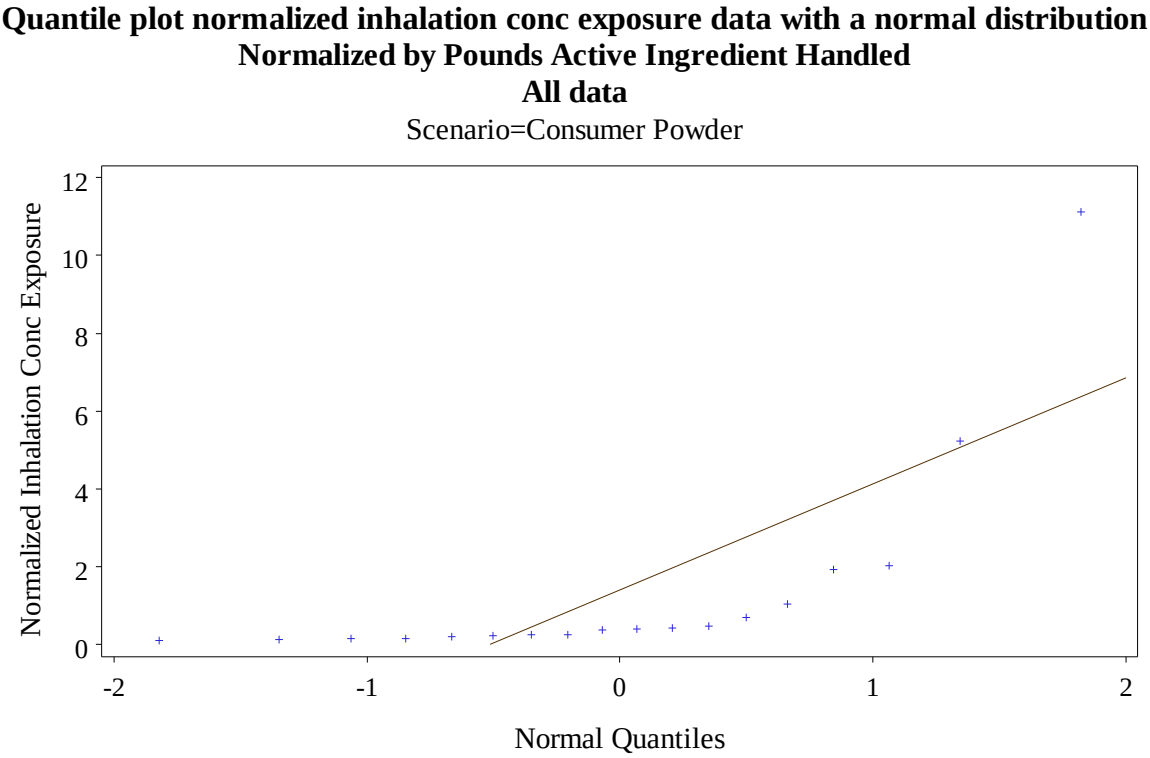

Figure 19. Empirical quantile plot for Inhalation Concentration, Consumer Powder, All data, with a normal distribution

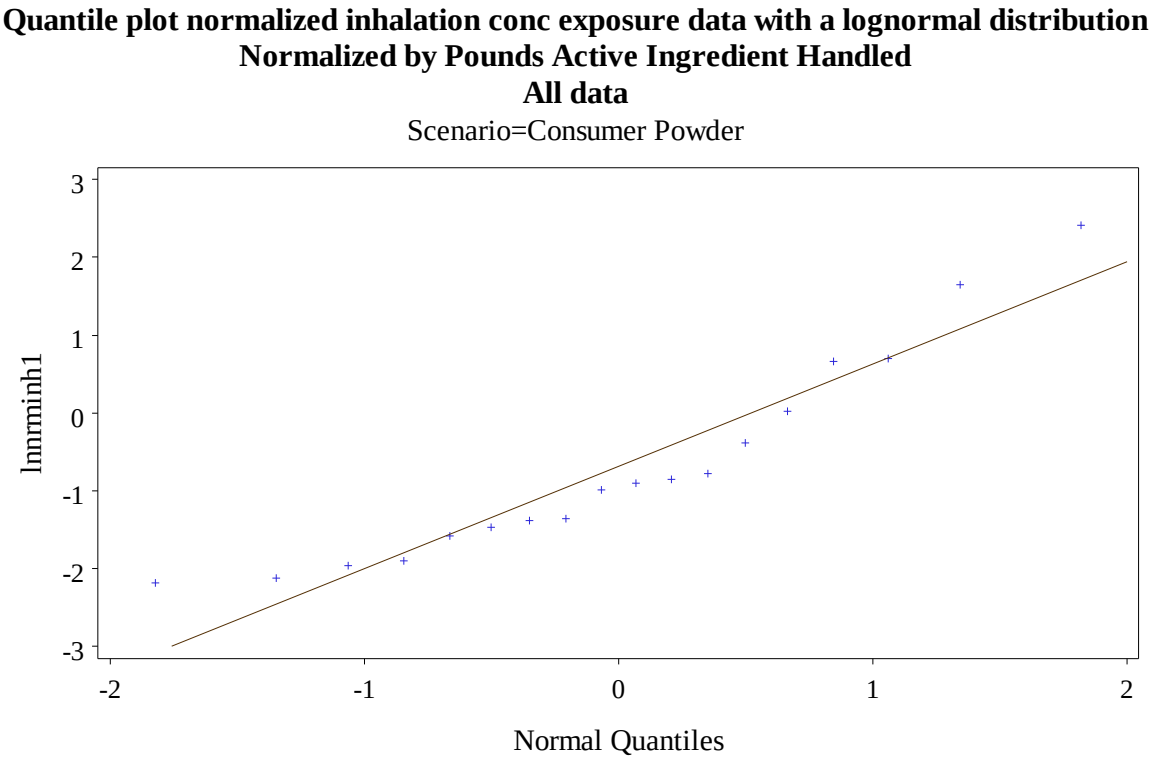

Figure 20. Empirical quantile plot for Inhalation Concentration, Consumer Powder, All data, with a lognormal distribution

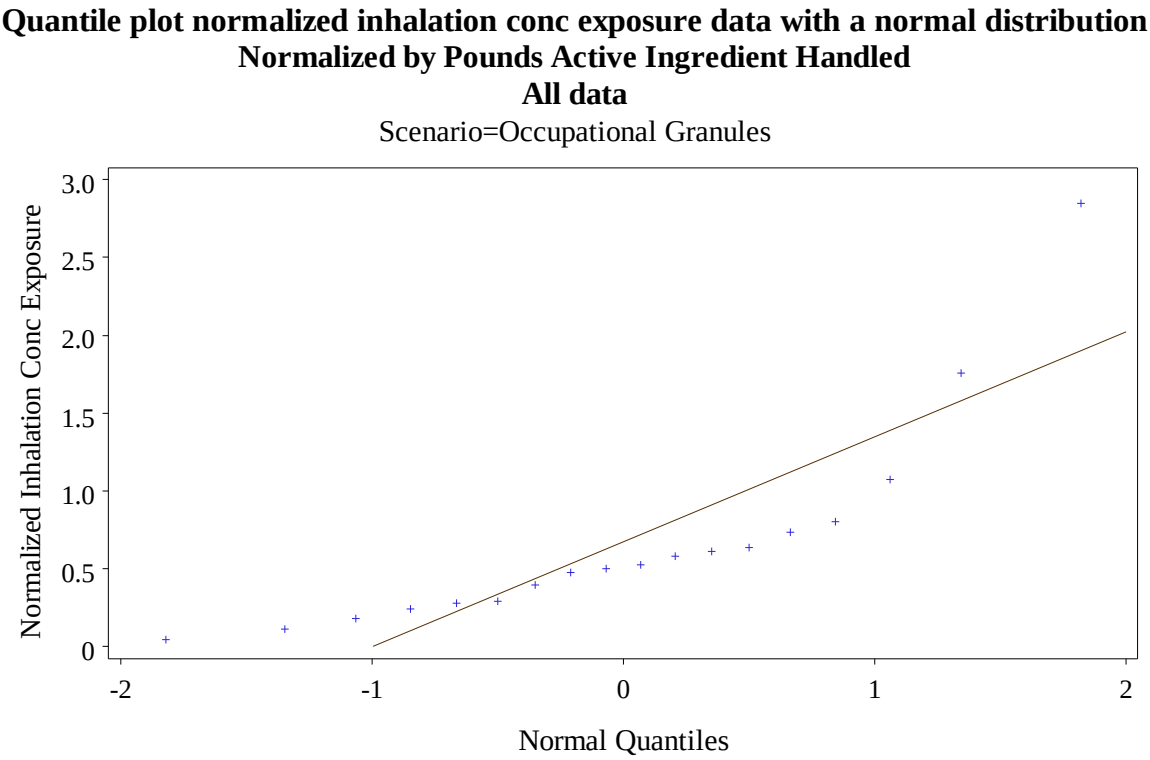

Figure 21. Empirical quantile plot for Inhalation Concentration, Occupational Granules, All data, with a normal distribution

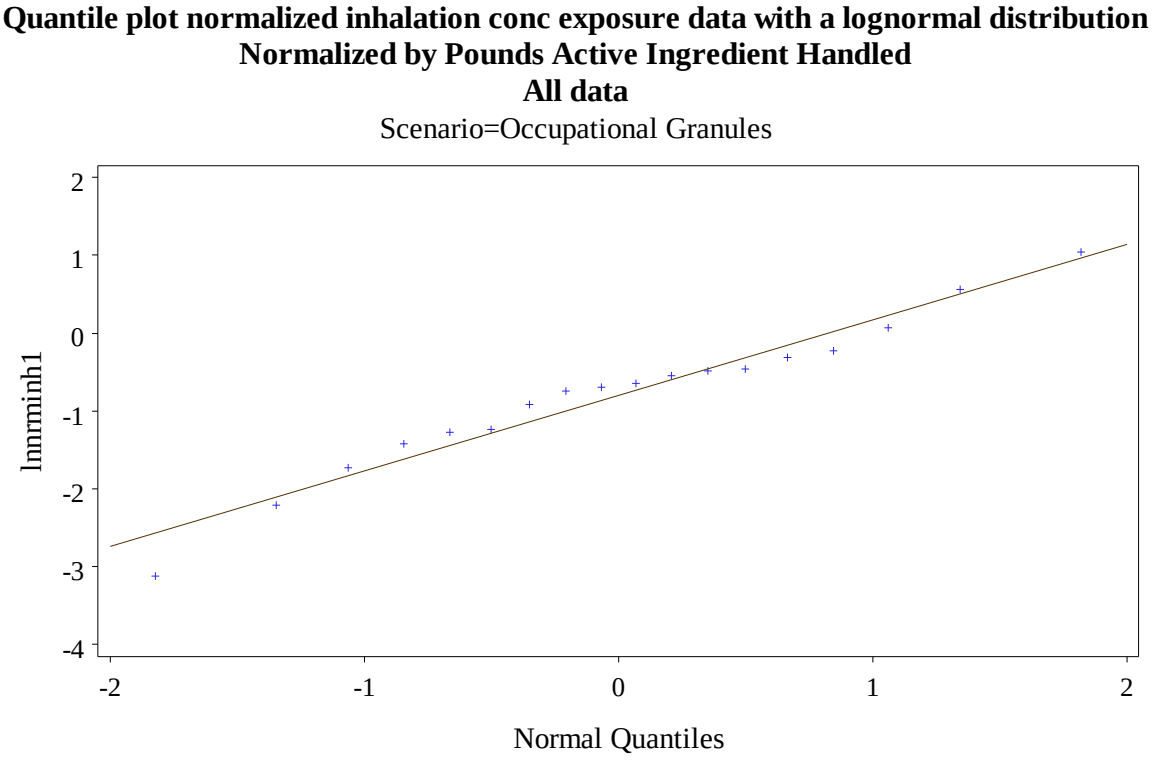

Figure 22. Empirical quantile plot for Inhalation Concentration, Occupational Granules, All data, with a lognormal distribution

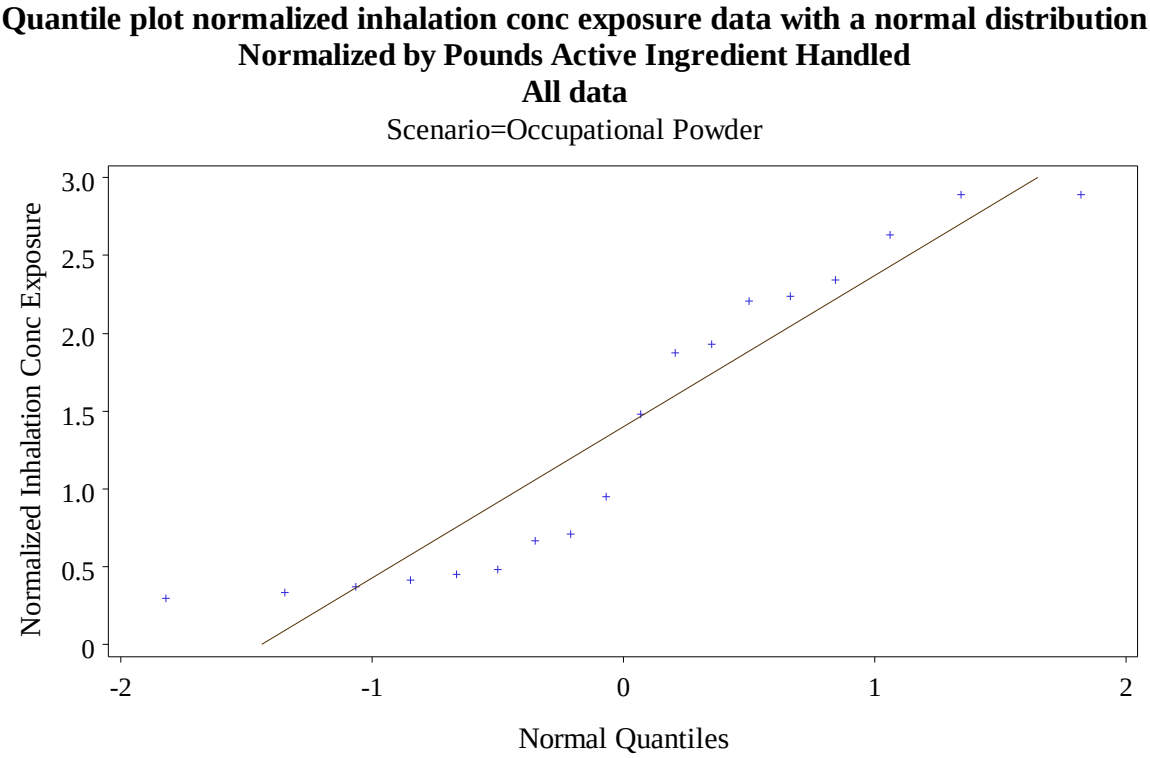

Figure 23. Empirical quantile plot for Inhalation Concentration, Occupational Powder, All data, with a normal distribution

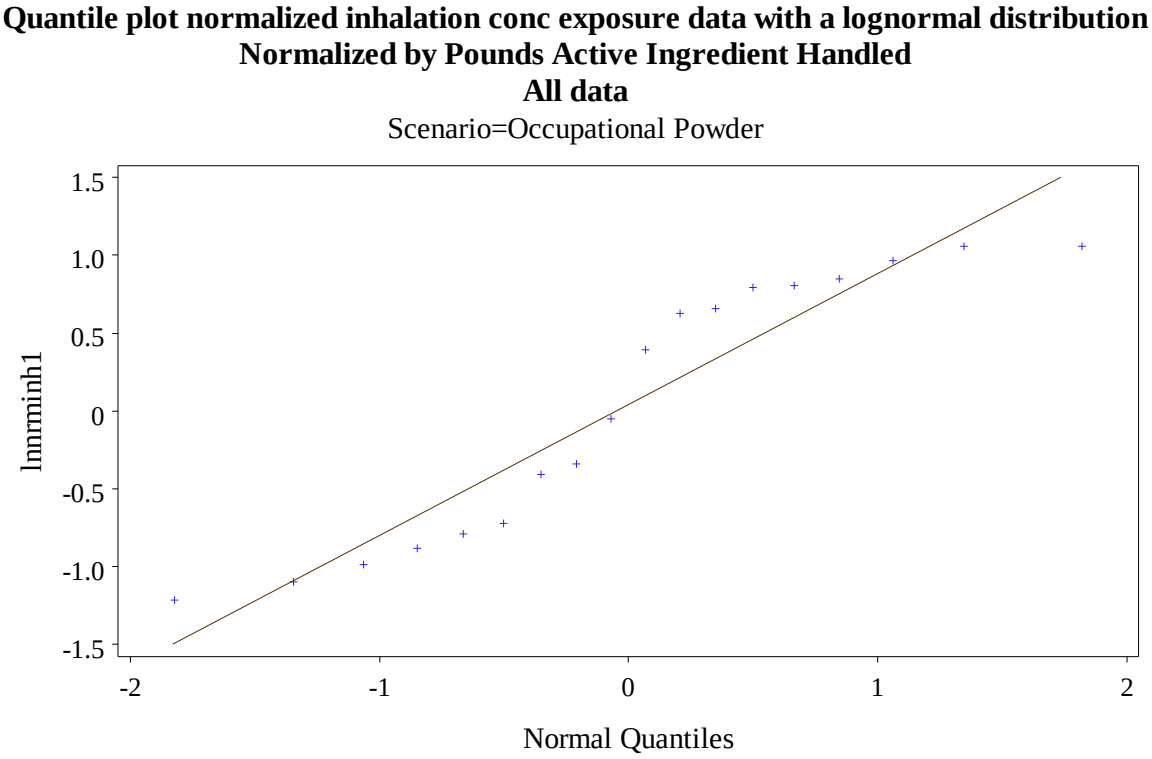

Figure 24. Empirical quantile plot for Inhalation Concentration, Occupational Powder, All data, with a lognormal distribution

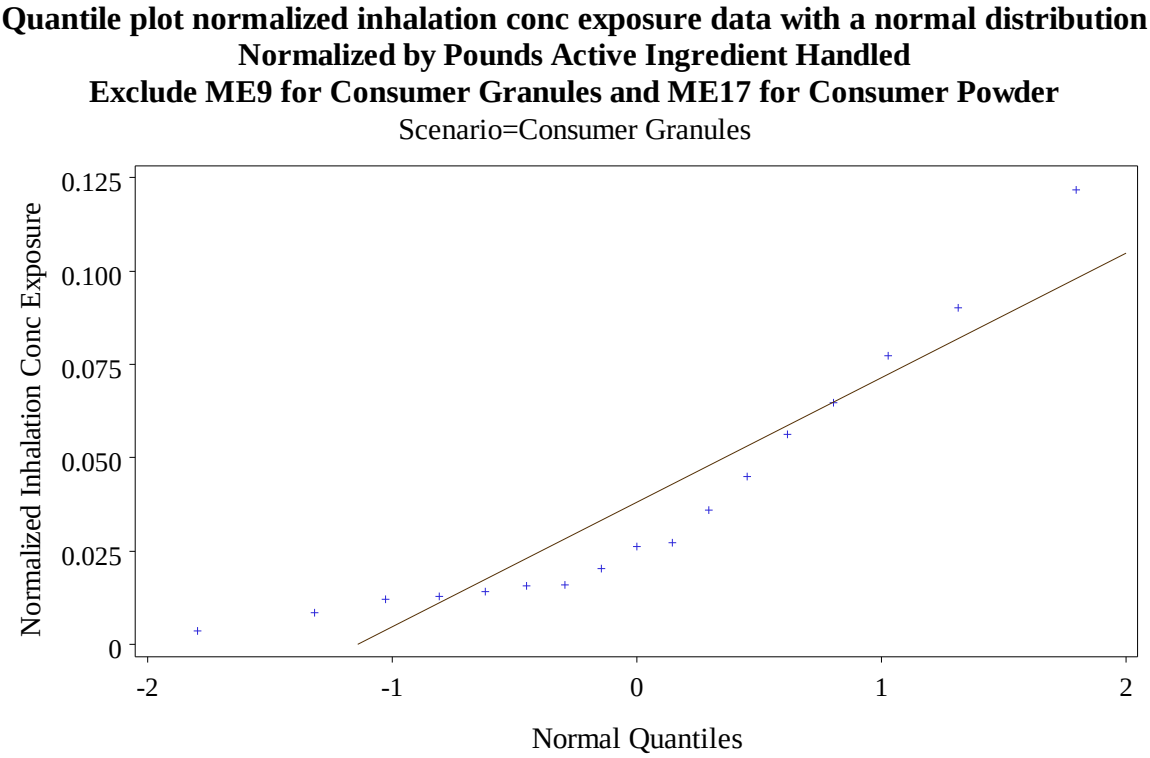

Figure 25. Empirical quantile plot for Inhalation Concentration, Consumer Granules, Exc. ME 9, with a normal distribution

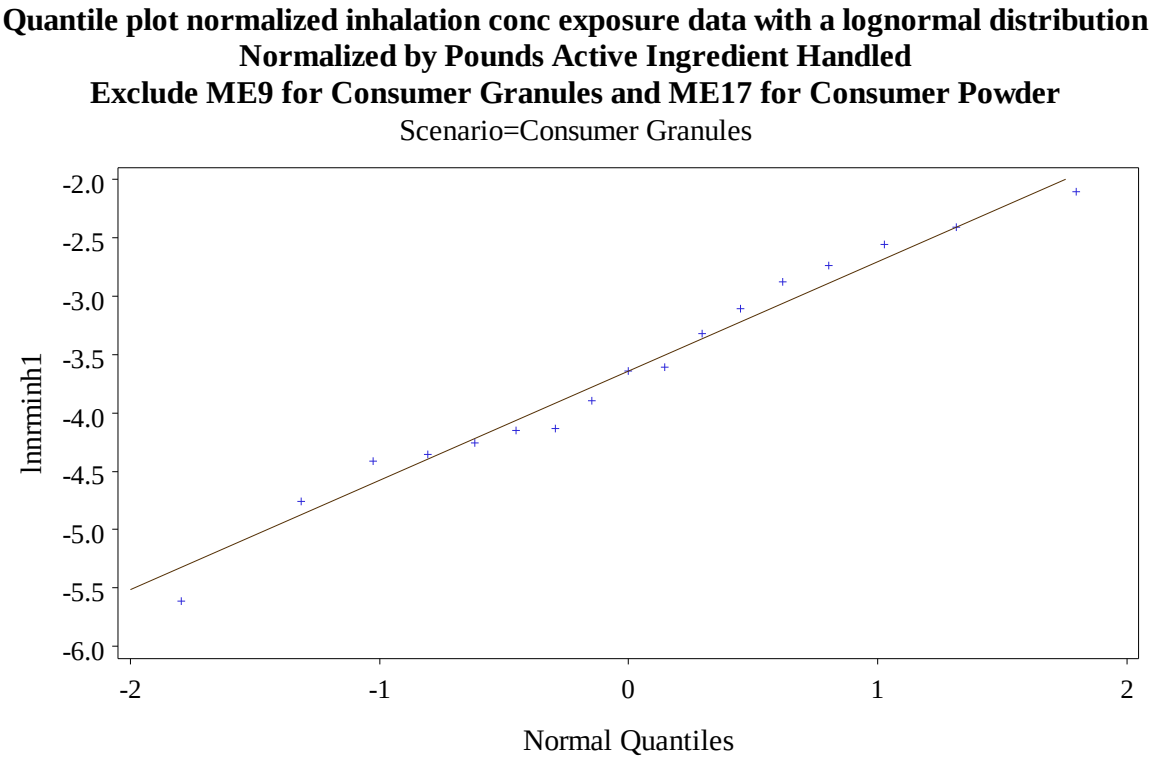

Figure 26. Empirical quantile plot for Inhalation Concentration, Consumer Granules, Exc. ME 9, with a lognormal distribution

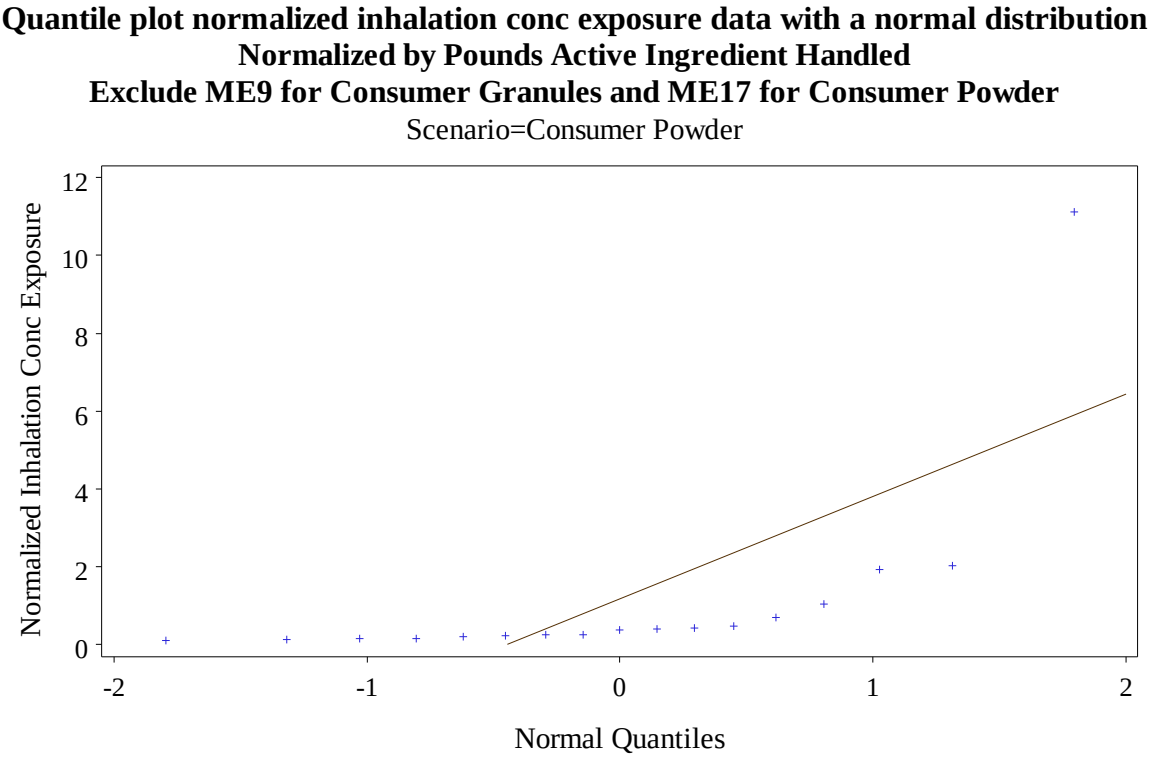

Figure 27. Empirical quantile plot for Inhalation Concentration, Consumer Powder, Exc. ME 17, with a normal distribution

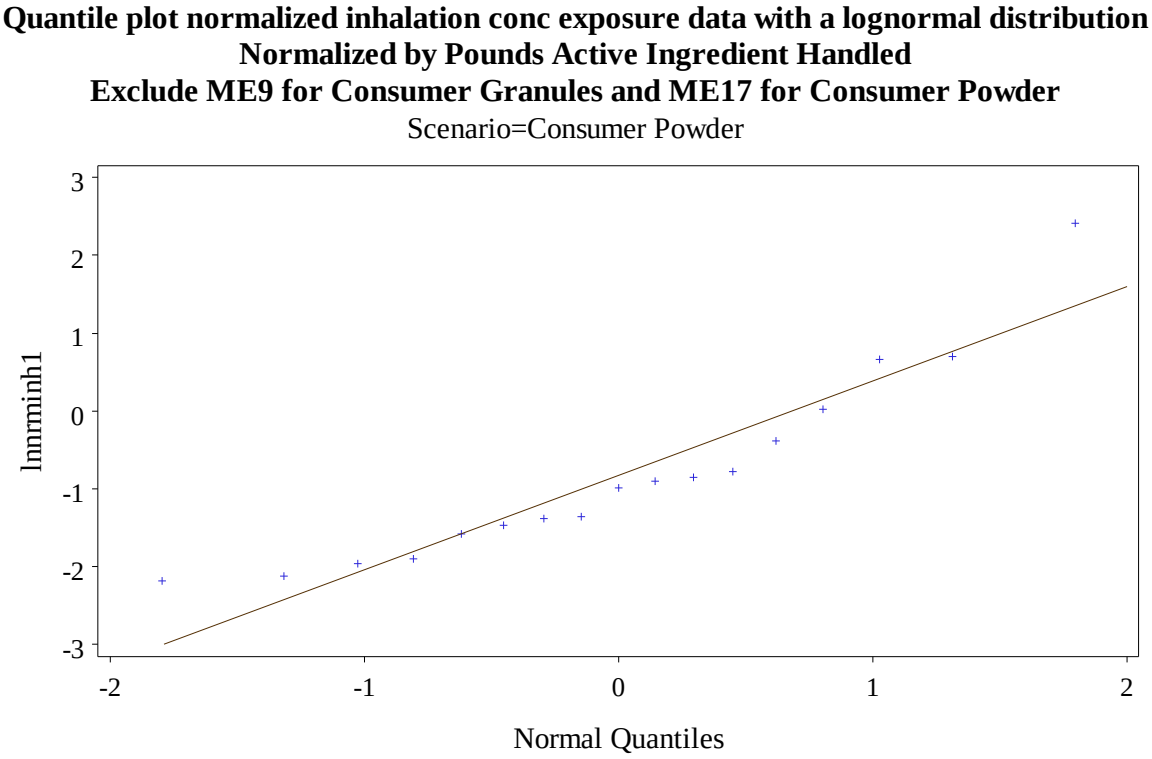

Figure 28. Empirical quantile plot for Inhalation Concentration, Consumer Powder, Exc. ME 17, with a lognormal distribution

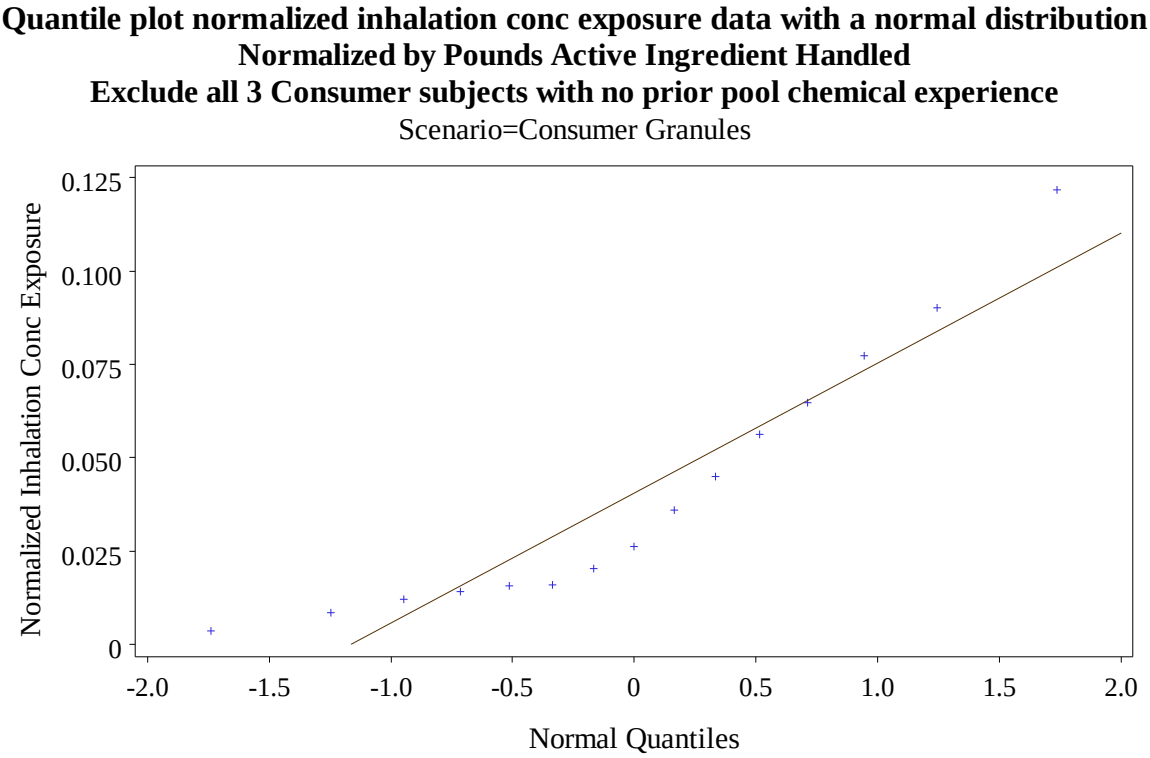

Figure 29. Empirical quantile plot for Inhalation Concentration, Consumer Granules, Experienced consumers, with a normal distribution

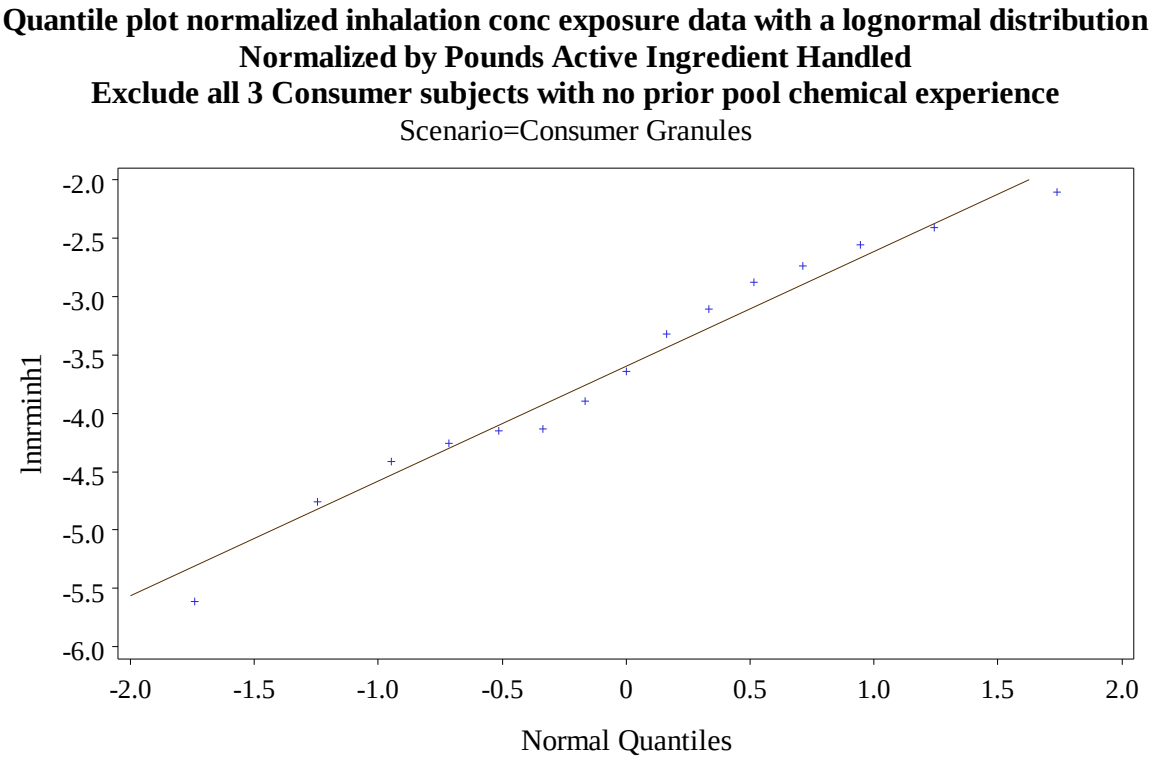

Figure 30. Empirical quantile plot for Inhalation Concentration, Consumer Granules, Experienced consumers, with a lognormal distribution

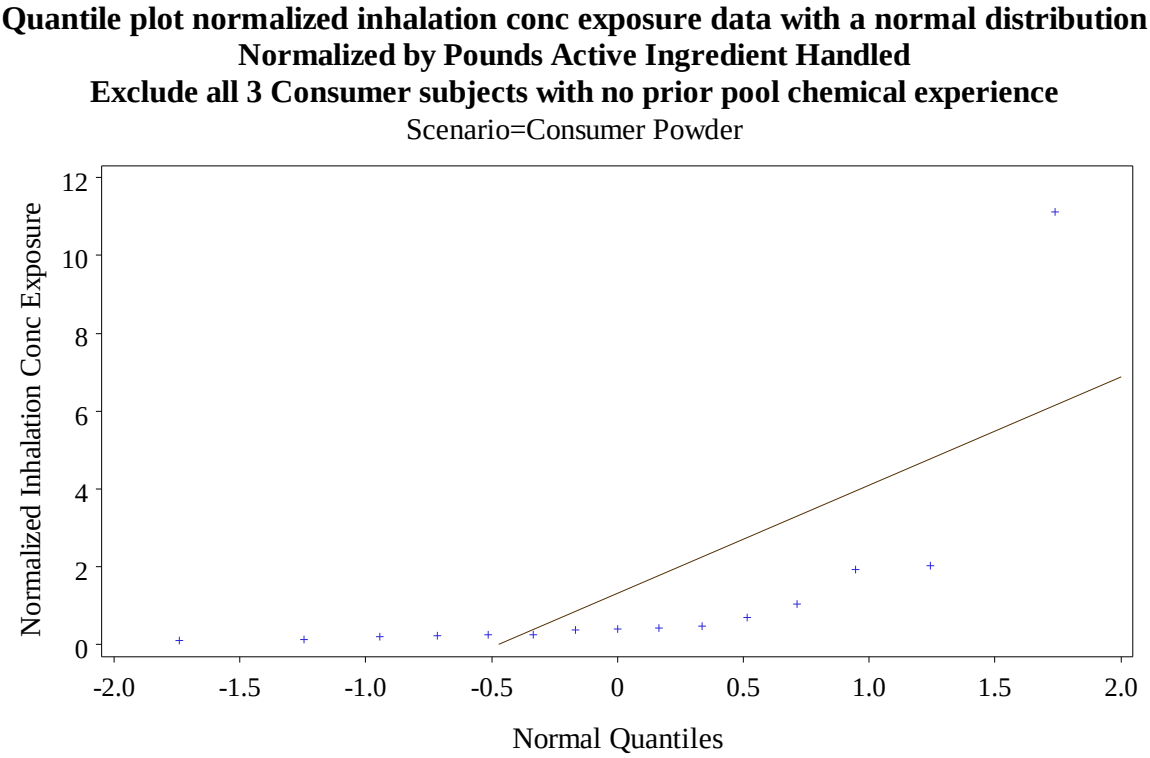

Figure 31. Empirical quantile plot for Inhalation Concentration, Consumer Powder, Experienced consumers, with a normal distribution

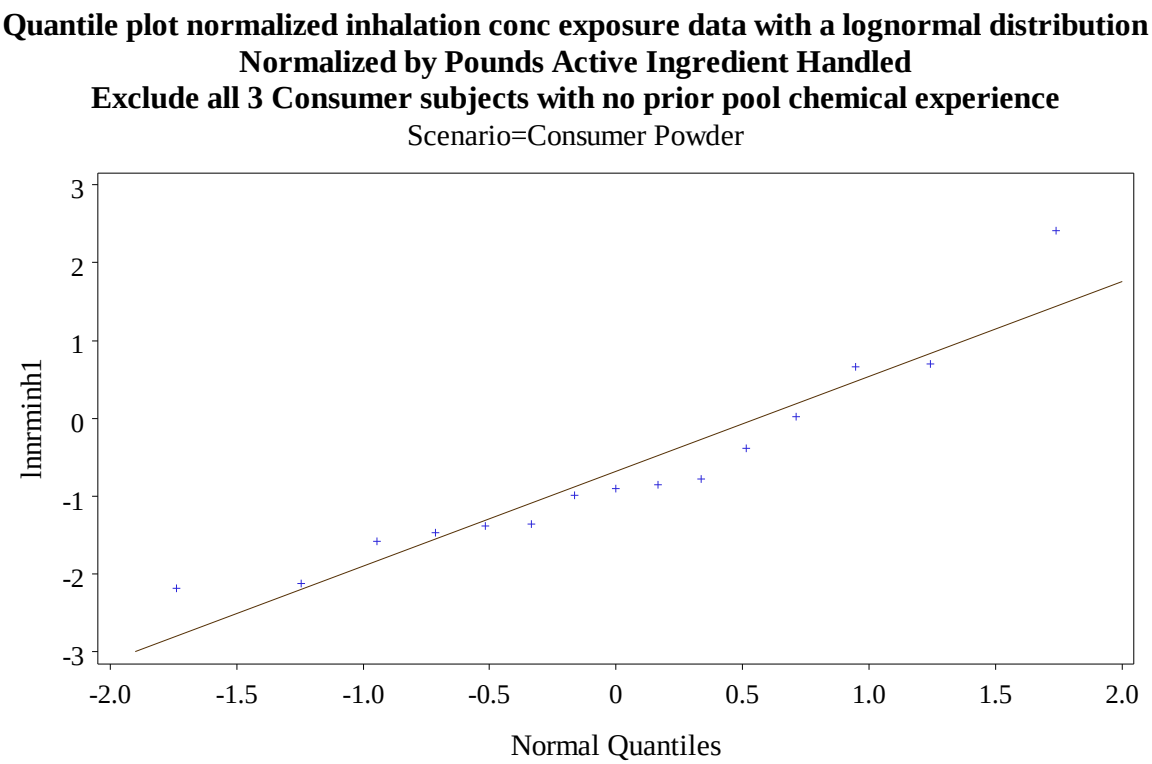

Figure 32. Empirical quantile plot for Inhalation Concentration, Consumer Powder, Experienced consumers, with a lognormal distribution

8. Log-log-Linearity Analyses and Estimated Log-log Slopes

The use of the normalized or unit exposure is based on the assumption that the exposure is proportional to the normalizing variable pounds of active ingredient handled. Exact proportionality is defined as

Exposure = K × Pounds of Active Ingredient,

where K is the proportionality constant. Exact proportionality implies that

Normalized Exposure = Exposure / Pounds of Active Ingredient = K,

so that if the pounds of active ingredient is doubled, then the exposure is exactly doubled, which is not a reasonable assumption due to the variability of exposure for any given amount of active ingredient. Instead of exact proportionality we allow for random multiplicative error terms, which do not depend on the amount of active ingredient, so that

Exposure = K × Pounds of Active Ingredient × Multiplicative Errors, or

Normalized Exposure = K × Multiplicative Errors.

Since the above quantile plots generally support the assumption that the normalized exposure is lognormally distributed, we can take natural logarithms of both sides to get a log-log-linear model of the form

Log (Exposure) = Intercept + 1 × Log (Pounds of Active Ingredient) + Error Terms.

The statistical analyses of log-log-linearity, previously referred to as proportionality, is based on the following more general log-log-linear statistical model:

Linear Model

Log (Exposure) = Intercept + Slope × Log (Pounds of Active Ingredient) + Random Error.

The Random Error terms are assumed to be normally distributed with a mean of zero and a variance of Vareror. The error terms are also assumed to be independent of the amount of active ingredient, which is the explanatory variable in this regression model. The values of Intercept, Slope, and Vareror are parameters of the fitted model. This linear model is for the Exposure rather than the Normalized Exposure (Exposure / AI).

Using this model, taking exponentials of both sides gives

Exposure = $e^{\text{Intercept}} \times (\text{Pounds of Active Ingredient})^{\text{Slope}} \times e^{\text{Random Error}}$, so that

E{Exposure | AI} = Expected Exposure Given the Pounds of Active Ingredient

= C × (Pounds of Active Ingredient)$^{\text{Slope}}$, where

C = Expected Value $\{e^{\text{Intercept}} \times e^{\text{Random Error}}\} = e^{\text{Intercept}} \times e^{\text{Varerror}/2}$

The value of E{Exposure | AI} is the arithmetic mean of the distribution of exposures for a future set of randomly selected consumers or workers that are all pouring exactly the same amount of active ingredient, AI. The parameters Intercept and Varerror are unknown, but are estimated by fitting the linear model to the solid pour data.

Therefore, the expected exposure given the AI will be proportional to the pounds of active ingredient if and only if the Slope in the linear model equals 1. Note that the proportionality constant is C, which is very different to the estimated value of Slope.

Lognormal Model

If the value of Slope in the linear model is 1, then

Log (Exposure) = Intercept + 1 × Log (Pounds of Active Ingredient) + Random Error,

so that

Log (Normalized Exposure) = Log(Exposure / Pounds of Active Ingredient)

= Intercept + Random Error,

This statistical model is exactly the same as the lognormal simple random sampling model that was defined above.

The same calculations that we used for the linear model give

E{Exposure | AI} = Expected Exposure Given the Pounds of Active Ingredient

= C* × (Pounds of Active Ingredient), where

C* = Expected Value $\{e^{Intercept^* \times Random\ Error}\} = e^{Intercept^*} \times e^{Varerror^*/2}$

These parameters are shown with asterisks to emphasize that they will in general be different from the ones for the model with a slope parameter not necessarily equal to 1.

Test for log-log-linearity with slope 1

Proportionality, or log-log-linearity with slope 1, of exposure to the pounds of active ingredient is statistically modeled by assuming a Slope equal to 1 in the linear model.

Possible alternative models include the same formulation with a Slope of zero, implying that the exposure does not depend upon the amount of active ingredient handled, even though the amount of active ingredient handled varied between the subjects as part of the study design. Other possible models include the same model with a slope not equal to zero or one, the quadratic models discussed below, or models with more complicated relationships between the exposure and the experimental conditions. To evaluate and test whether the slope is zero, one, or other possible values, we fitted the above linear model and computed confidence intervals for the slope.

Table 37 to Table 40 (one for each scenario) show the 95% confidence intervals for the slope calculated from the above linear model. A confidence interval that includes one but not zero supports the use of unit exposures. A confidence interval that includes zero but not one suggests that the exposure does not depend on the amount of active ingredient

handled. A confidence interval that includes both zero and one suggests that either the basic statistical model is incorrect or there are not enough data to statistically infer whether the slope is zero or one. Note that, because the inhalation or respirable dose is mathematically an exact multiple of the corresponding inhalation or respirable TWA, the estimated slopes and confidence intervals are exactly the same. For the Consumer Granules and Consumer Powder scenarios, results are presented for all data, for data without the potential outlier, and for data for experienced consumers only. These tables also show the widths of the confidence intervals used to evaluate the second benchmark for post-hoc power discussed in the next sub-section. These tables also show the values of the threshold amount of active ingredient and the corresponding estimated exposure, to be described and discussed below in Section 10. Threshold values were not computed for the censored data models.

For the Consumer Granules scenario there were some non-detects for all exposure routes. For the Consumer Powder scenario there were some non-detects for the inhalation exposure routes. The rows marked "Substitute ½ LOQ" calculate the slope estimates after replacing each non-detect residue by half the LOQ. The rows marked "Censored data MLE" calculate the slope estimates for the linear model using a censored maximum likelihood statistical method and the lower and upper bounds for each non-detect that were calculated as described in Section 4. This procedure was implemented using the LIFEREG SAS procedure.

Table 37. 95 percent confidence intervals for the slope of log exposure versus log pounds active ingredient handled for Consumer Granules

Exposure Route	Treatment of Non-detects	Data	Estimate	Lower	Upper	Width	Threshold	Exposure
Long Dermal (mg)	Substitute ½ LOQ	All	0.34	-0.28	0.96	1.24	6.125	5.552
		Exc. ME 9	0.33	-0.12	0.78	0.90	5.592	2.319
		Experienced	0.29	-0.18	0.76	0.94	4.740	2.027
	Censored data MLE	All	0.34	-0.20	0.88	1.08		
		Exc. ME 9	0.33	-0.06	0.72	0.77		
		Experienced	0.29	-0.10	0.69	0.79		
Short Dermal (mg)	Substitute ½ LOQ	All	0.41	-0.18	1.00	1.19	6.545	12.264
		Exc. ME 9	0.41	-0.04	0.85	0.89	6.019	5.707
		Experienced	0.38	-0.10	0.87	0.96	5.260	5.458
	Censored data MLE	All	0.41	-0.11	0.93	1.03		
		Exc. ME 9	0.41	0.02	0.79	0.77		
		Experienced	0.38	-0.02	0.79	0.81		
Long Short Dermal (mg)	Substitute ½ LOQ	All	0.48	-0.13	1.09	1.22	7.076	7.719
		Exc. ME 9	0.47	0.03	0.92	0.89	6.447	3.314
		Experienced	0.44	-0.03	0.92	0.95	5.612	3.011
	Censored data MLE	All	0.48	-0.05	1.01	1.06		
		Exc. ME 9	0.47	0.09	0.86	0.77		
		Experienced	0.44	0.04	0.84	0.80		
Hands Only (mg)	Substitute ½ LOQ	All	0.41	-0.28	1.09	1.37	6.781	6.034

Exposure Route	Treatment of Non-detects	Data	Estimate	Lower	Upper	Width	Threshold	Exposure
		Exc. ME 9	0.40	-0.12	0.93	1.05	6.158	2.373
		Experienced	0.36	-0.19	0.92	1.11	5.270	2.079
	Censored data MLE	All	0.41	-0.19	1.01	1.20		
		Exc. ME 9	0.40	-0.05	0.86	0.91		
		Experienced	0.36	-0.10	0.83	0.93		
Inhalation Concentration (mg/m^3)	Substitute ½ LOQ	All	0.76	0.40	1.12	0.72	8.695	0.374
		Exc. ME 9	0.76	0.40	1.12	0.72	8.600	0.349
		Experienced	0.76	0.37	1.15	0.78	8.041	0.356
	Censored data MLE	All	0.76	0.44	1.08	0.63		
		Exc. ME 9	0.76	0.45	1.07	0.63		
		Experienced	0.76	0.43	1.09	0.66		
Inhalation Dose (mg)	Substitute ½ LOQ	All	0.77	0.34	1.20	0.85	9.180	0.026
		Exc. ME 9	0.77	0.41	1.13	0.72	8.868	0.018
		Experienced	0.73	0.37	1.09	0.72	7.607	0.014
	Censored data MLE	All	0.77	0.40	1.14	0.74		
		Exc. ME 9	0.77	0.45	1.08	0.62		
		Experienced	0.73	0.43	1.04	0.61		
Inhalation 8-hour TWA (mg/m^3)	Substitute ½ LOQ	All	0.77	0.34	1.20	0.85	9.180	0.0033
		Exc. ME 9	0.77	0.41	1.13	0.72	8.868	0.0023
		Experienced	0.73	0.37	1.09	0.72	7.607	0.0018
	Censored data MLE	All	0.77	0.40	1.14	0.74		
		Exc. ME 9	0.77	0.45	1.08	0.62		
		Experienced	0.73	0.43	1.04	0.61		
Respirable Concentration (mg/m^3)	Substitute ½ LOQ	All	0.76	0.42	1.10	0.67	8.566	0.0088
		Exc. ME 9	0.76	0.42	1.10	0.68	8.489	0.0084
		Experienced	0.77	0.40	1.15	0.75	8.135	0.0089
	Censored data MLE	All	0.87	0.53	1.21	0.69		
		Exc. ME 9	0.88	0.53	1.22	0.69		
		Experienced	0.90	0.53	1.27	0.74		
Respirable Dose (mg)	Substitute ½ LOQ	All	0.77	0.41	1.12	0.71	8.751	0.00053
		Exc. ME 9	0.77	0.48	1.05	0.57	8.318	0.00039

Exposure Route	Treatment of Non-detects	Data	Estimate	Lower	Upper	Width	Threshold	Exposure
		Experienced	0.75	0.50	0.99	0.49	7.329	0.00029
	Censored data MLE	All	0.77	0.42	1.12	0.70		
		Exc. ME 9	0.73	0.47	1.00	0.54		
		Experienced	0.70	0.48	0.92	0.44		
Respirable 8-hour TWA (mg/m^3)	Substitute ½ LOQ	All	0.77	0.41	1.12	0.71	8.751	0.000066
		Exc. ME 9	0.77	0.48	1.05	0.57	8.318	0.000048
		Experienced	0.75	0.50	0.99	0.49	7.329	0.000036
	Censored data MLE	All	0.77	0.42	1.12	0.70		
		Exc. ME 9	0.73	0.47	1.00	0.54		
		Experienced	0.70	0.48	0.92	0.44		

Table 38. 95 percent confidence intervals for the slope of log exposure versus log pounds active ingredient handled for Consumer Powder

Exposure Route	Treatment of Non-detects	Data	Estimate	Lower	Upper	Width	Threshold	Exposure
Long Dermal (mg)	N/A	All	0.47	0.16	0.77	0.61	1.950	6.690
		Exc. ME 17	0.57	0.29	0.85	0.56	2.560	5.848
		Experienced	0.60	0.28	0.92	0.64	2.977	6.674
Short Dermal (mg)	N/A	All	0.59	0.22	0.96	0.74	2.356	22.603
		Exc. ME 17	0.66	0.29	1.04	0.75	3.052	22.804
		Experienced	0.68	0.26	1.11	0.84	3.521	28.091
Long Short Dermal (mg)	N/A	All	0.57	0.24	0.90	0.66	2.251	11.635
		Exc. ME 17	0.67	0.36	0.99	0.63	2.959	10.743
		Experienced	0.71	0.35	1.06	0.70	3.493	12.791
Hands Only (mg)	N/A	All	0.49	0.14	0.84	0.70	2.053	6.384
		Exc. ME 17	0.61	0.28	0.94	0.66	2.737	5.529
		Experienced	0.65	0.27	1.03	0.76	3.256	6.435
Inhalation Concentration (mg/m^3)	Substitute ½ LOQ	All	0.48	0.13	0.83	0.70	2.012	2.395
		Exc. ME 17	0.55	0.19	0.91	0.72	2.574	2.349
		Experienced	0.43	0.09	0.77	0.68	2.409	2.563
	Censored data MLE	All	0.48	0.17	0.78	0.61		
		Exc. ME 17	0.55	0.24	0.87	0.63		
		Experienced	0.43	0.14	0.72	0.58		

Exposure Route	Treatment of Non-detects	Data	Estimate	Lower	Upper	Width	Threshold	Exposure
Inhalation Dose (mg)	Substitute ½ LOQ	All	0.75	0.42	1.09	0.67	2.981	0.130
		Exc. ME 17	0.84	0.50	1.17	0.67	3.961	0.141
		Experienced	0.78	0.42	1.13	0.71	3.914	0.156
	Censored data MLE	All	0.75	0.46	1.04	0.58		
		Exc. ME 17	0.84	0.54	1.13	0.58		
		Experienced	0.78	0.48	1.08	0.60		
Inhalation 8-hour TWA (mg/m^3)	Substitute ½ LOQ	All	0.75	0.42	1.09	0.67	2.981	0.0162
		Exc. ME 17	0.84	0.50	1.17	0.67	3.961	0.0176
		Experienced	0.78	0.42	1.13	0.71	3.914	0.0195
	Censored data MLE	All	0.75	0.46	1.04	0.58		
		Exc. ME 17	0.84	0.54	1.13	0.58		
		Experienced	0.78	0.48	1.08	0.60		
Respirable Concentration (mg/m^3)	Substitute ½ LOQ	All	0.32	0.07	0.57	0.50	1.590	0.0055
		Exc. ME 17	0.35	0.08	0.62	0.54	1.948	0.0055
		Experienced	0.32	0.02	0.62	0.60	2.094	0.0064
	Censored data MLE	All	0.33	0.09	0.57	0.48		
		Exc. ME 17	0.37	0.12	0.63	0.52		
		Experienced	0.34	0.05	0.62	0.57		
Respirable Dose (mg)	Substitute ½ LOQ	All	0.59	0.32	0.87	0.55	2.277	0.00028
		Exc. ME 17	0.64	0.34	0.93	0.58	2.792	0.00030
		Experienced	0.67	0.34	1.00	0.66	3.268	0.00039
	Censored data MLE	All	0.58	0.34	0.83	0.49		
		Exc. ME 17	0.63	0.37	0.89	0.53		
		Experienced	0.66	0.37	0.96	0.59		
Respirable 8-hour TWA (mg/m^3)	Substitute ½ LOQ	All	0.59	0.32	0.87	0.55	2.277	0.000036
		Exc. ME 17	0.64	0.34	0.93	0.58	2.792	0.000038
		Experienced	0.67	0.34	1.00	0.66	3.268	0.000044
	Censored data MLE	All	0.58	0.34	0.83	0.49		
		Exc. ME 17	0.63	0.37	0.89	0.53		
		Experienced	0.66	0.37	0.96	0.59		

Table 39. 95 percent confidence intervals for the slope of log exposure versus log pounds active ingredient handled for Occupational Granules

Exposure Route	Treatment of Non-detects	Data	Estimate	Lower	Upper	Width	Threshold	Exposure
Long Dermal (mg)	N/A	All	1.39	0.88	1.89	1.01	36.731	1.802
Short Dermal (mg)	N/A	All	0.96	0.34	1.58	1.25	54.692	34.233
Long Short Dermal (mg)	N/A	All	0.98	0.17	1.78	1.61	124.445	59.835
Hands Only (mg)	N/A	All	0.94	0.27	1.61	1.34	49.023	0.699
Inhalation Concentration (mg/m^3)	N/A	All	1.17	0.39	1.96	1.57	30.587	22.068
Inhalation Dose (mg)	N/A	All	1.51	0.69	2.33	1.64	36.537	2.865
Inhalation 8-hour TWA (mg/m^3)	N/A	All	1.51	0.69	2.33	1.64	36.537	0.358
Respirable Concentration (mg/m^3)	N/A	All	1.38	0.66	2.10	1.44	35.450	1.007
Respirable Dose (mg)	N/A	All	1.71	0.94	2.49	1.54	39.034	0.126
Respirable 8-hour TWA (mg/m^3)	N/A	All	1.71	0.94	2.49	1.54	39.034	0.016

Table 40. 95 percent confidence intervals for the slope of log exposure versus log pounds active ingredient handled for Occupational Powder

Exposure Route	Treatment of Non-detects	Data	Estimate	Lower	Upper	Width	Threshold	Exposure
Long Dermal (mg)	N/A	All	0.69	0.10	1.27	1.17	29.508	6.671
Short Dermal (mg)	N/A	All	0.93	0.27	1.58	1.31	42.251	140.247
Long Short Dermal (mg)	N/A	All	0.85	0.04	1.66	1.62	37.597	103.301
Hands Only (mg)	N/A	All	0.56	-0.33	1.44	1.77	29.719	2.318
Inhalation Concentration (mg/m^3)	N/A	All	0.44	-0.09	0.97	1.06	26.665	39.503
Inhalation Dose (mg)	N/A	All	0.82	0.09	1.54	1.44	33.962	7.618
Inhalation 8-hour TWA (mg/m^3)	N/A	All	0.82	0.09	1.54	1.44	33.962	0.952

Exposure Route	Treatment of Non-detects	Data	Estimate	Lower	Upper	Width	Threshold	Exposure
Respirable Concentration (mg/m^3)	N/A	All	0.69	0.08	1.31	1.23	29.816	0.332
Respirable Dose (mg)	N/A	All	1.07	0.29	1.86	1.57	18.605	0.033
Respirable 8-hour TWA (mg/m^3)	N/A	All	1.07	0.29	1.86	1.57	18.605	0.0041

Table 37 gives the slopes for Consumer Granules. For dermal exposures, the slopes range from about 0.3 to 0.5 and, using all the data, the confidence intervals for the slope include 0 but (in most cases) not 1. Thus the assumption of independence was not rejected and the assumption of log-log-linearity with slope 1 was rejected. For inhalation exposures, the slopes are about 0.8 and in most cases the confidence intervals for the slope include 1 but not 0. Thus the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was not rejected.

Table 38 gives the slopes for Consumer Powder. The slopes range from 0.3 to 0.8 and the confidence intervals do not include 0. The confidence intervals include 1 in about half the cases. Thus the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was rejected in about half of the cases.

Table 39 gives the slopes for Occupational Granules. Most of the slopes are above 1 (ranging from about 0.9 to 1.7) and the confidence intervals include 1 but not 0. Thus the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was not rejected.

Table 40 gives the slopes for Occupational Powder. Most of the slopes are below 1 (ranging from 0.4 to 1.1) and the confidence intervals mostly include 1 but not 0. Thus the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was not rejected.

Confidence interval widths

Suppose that the study had a (post-hoc) power of at least 80% for detecting “proportionality” (i.e., log-log-linearity with a slope of 1) under the null hypothesis of independence (slope = 0). It follows that the confidence intervals have an approximate width of 1.4 or less. The results in Table 37 to Table 40 show that observed widths are all below 1.4 for the Consumer Scenarios but exceed 1.4 for about half of the cases for the Occupational Granules and Occupational Powder scenarios. The maximum width was 1.77 for the hands only exposure route for Occupational Powder. Therefore, based on the confidence intervals, the secondary objective of meeting the 80% power for detecting proportionality was not met for the Occupational Granules and Occupational Powder scenarios.

Quantile plots for residuals

To evaluate the fitted linear regression models we created quantile-quantile[1] plots of the studentized residuals for each fitted model. The residual is the observed value of log exposure minus the predicted value. The studentized residual is the residual divided by its standard error. For these analyses we used the internally studentized residual where the estimated standard error is calculated using all the data. An alternative approach that is sometimes preferred when checking for outliers in small samples is to use the externally studentized residual where the estimated standard error is calculated after excluding the data point. If the plotted points lie close to the straight line then the model assumptions for the linear model are supported. Furthermore, a standard rule of thumb identifies statistical outliers as cases where the studentized residual is above +3 or below −3 (a stricter criterion of ±2 is sometimes used, and more complex statistical outlier tests taking into account the sample size are also available). These quantile-quantile plots are for the Linear Model. Quantile-quantile plots for the Lognormal Model were presented in the even-numbered Figures 1-32 above, since in that case both the predicted values and the standard errors are the same for every ME.

The quantile-quantile plots for Short Dermal in the Consumer scenarios, the Long Dermal in the Occupational scenarios, and Inhalation Concentration exposure for all four scenarios are shown in Figure 33 to Figure 48 using the half LOQ substitution method for non-detect values. For Consumer Granules and Consumer Powder, the quantile-quantile plots are shown for all the data, for the data excluding the potential outliers, and for the experienced consumers only. Quantile-quantile plots for the other exposure metrics are not included here but can be made available upon request.

[1] These quantile plots compare the distribution of the studentized residuals to a standard normal distribution. Some authors prefer a more exact approach where the distribution of the studentized residuals is compared to a t distribution. That method is not easily available using current SAS software.

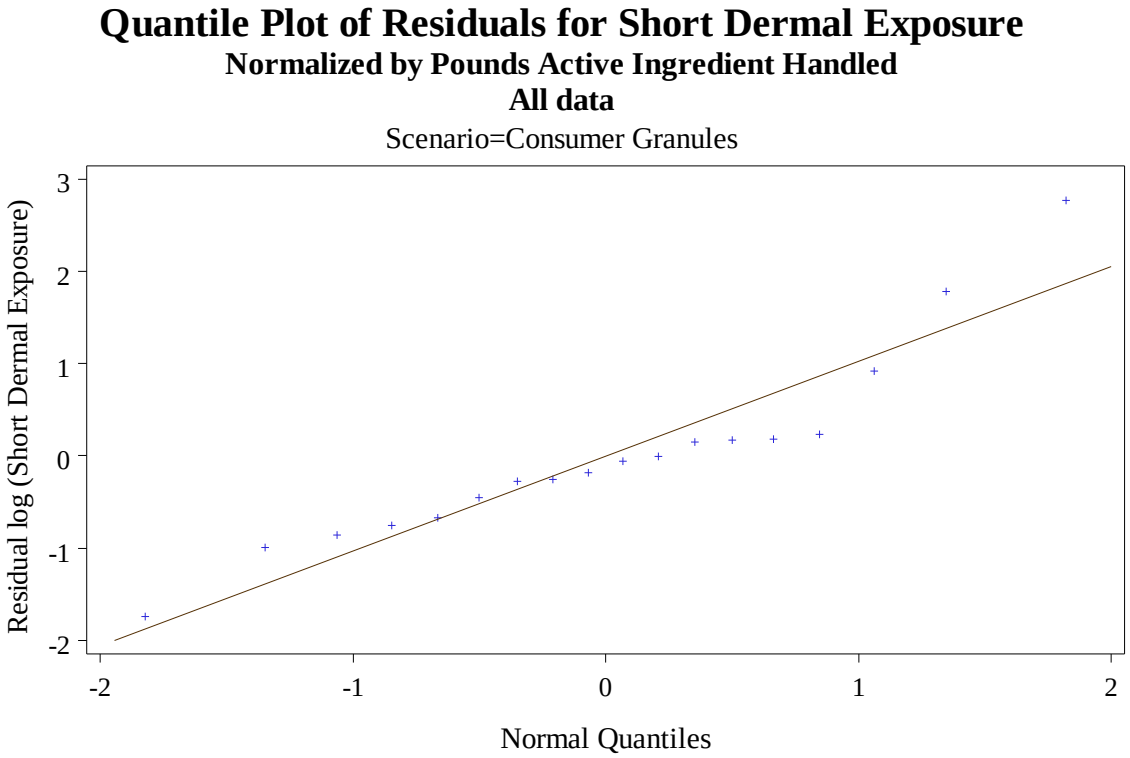

Figure 33. Quantile plot of residuals from linear model for Consumer Granules, Short Dermal, All data

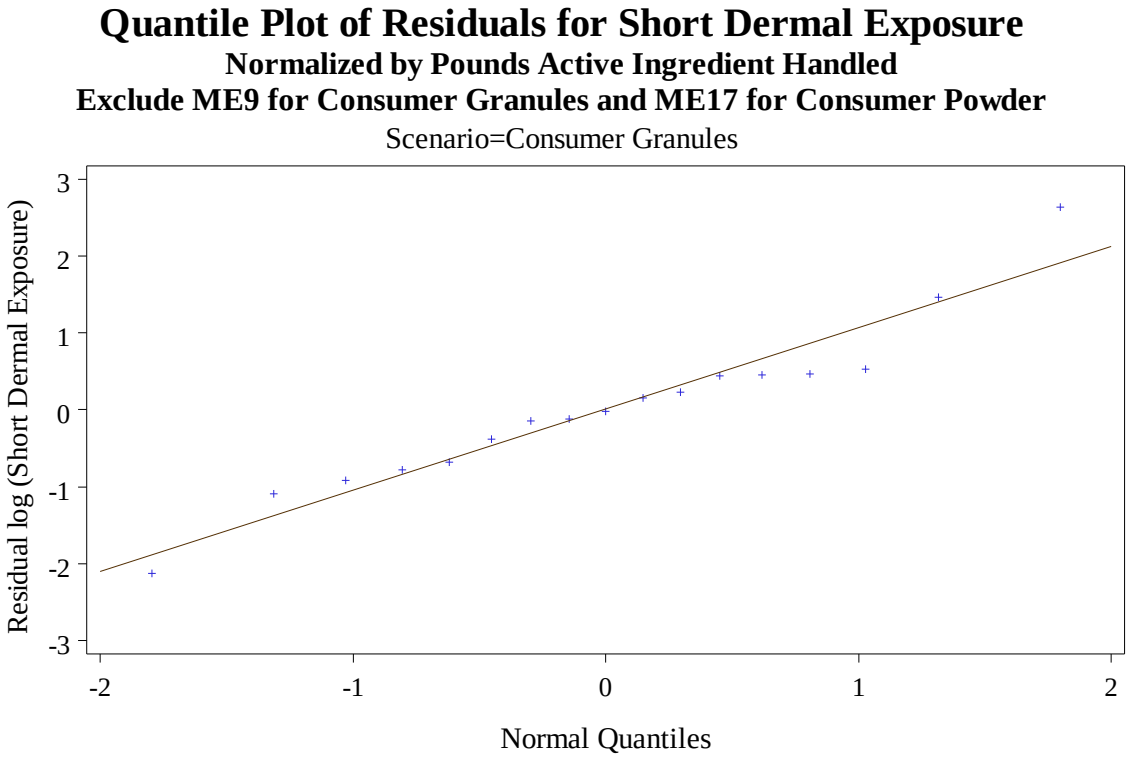

Figure 34. Quantile plot of residuals from linear model for Consumer Granules, Short Dermal, Exc. ME 9

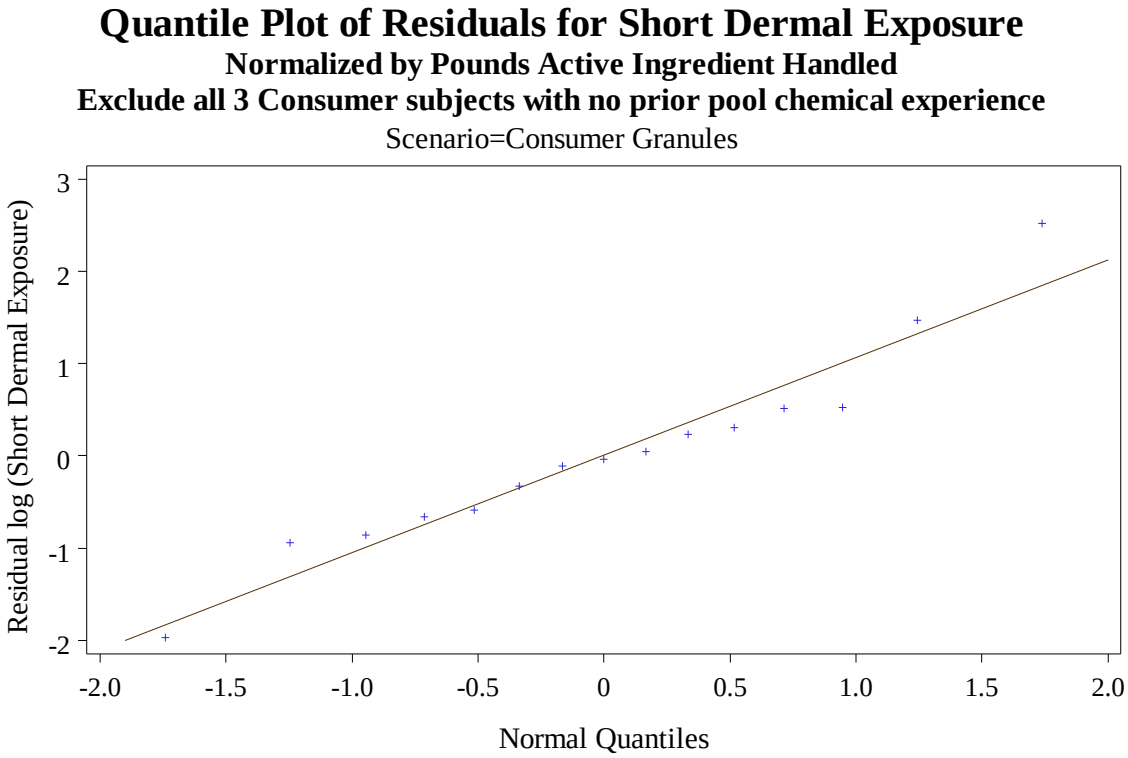

Figure 35. Quantile plot of residuals from linear model for Consumer Granules, Short Dermal, Experienced Consumers

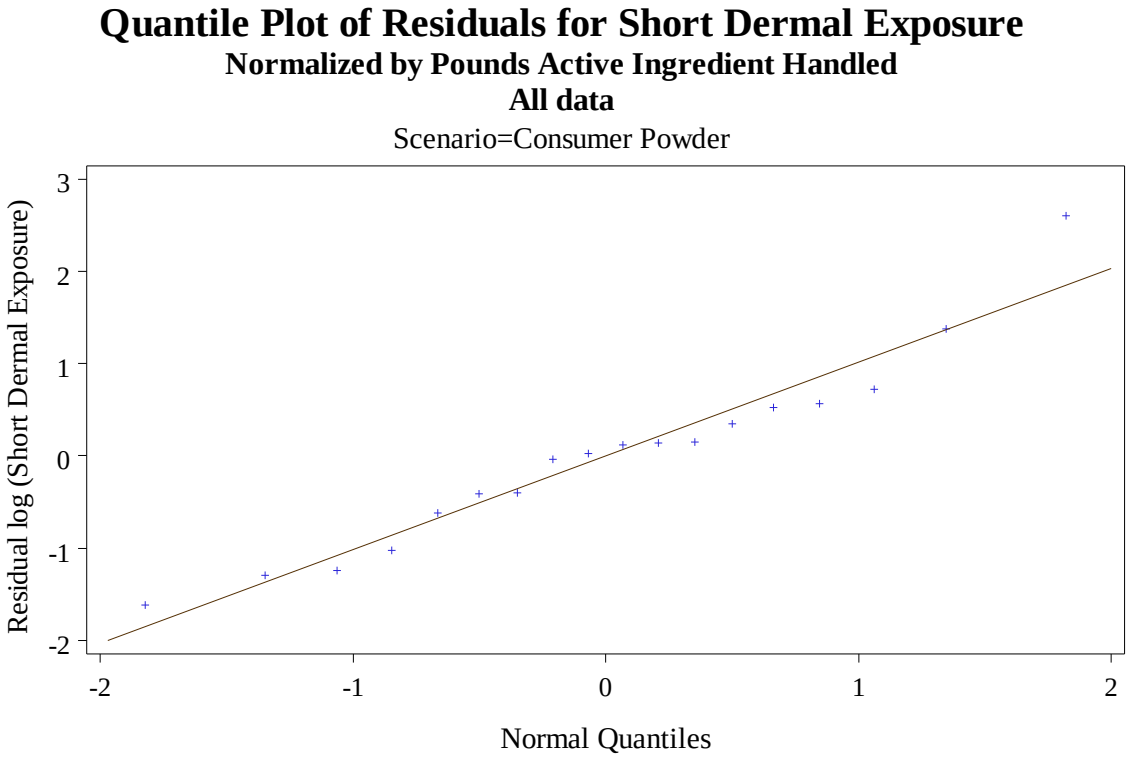

Figure 36. Quantile plot of residuals from linear model for Consumer Powder, Short Dermal, All data

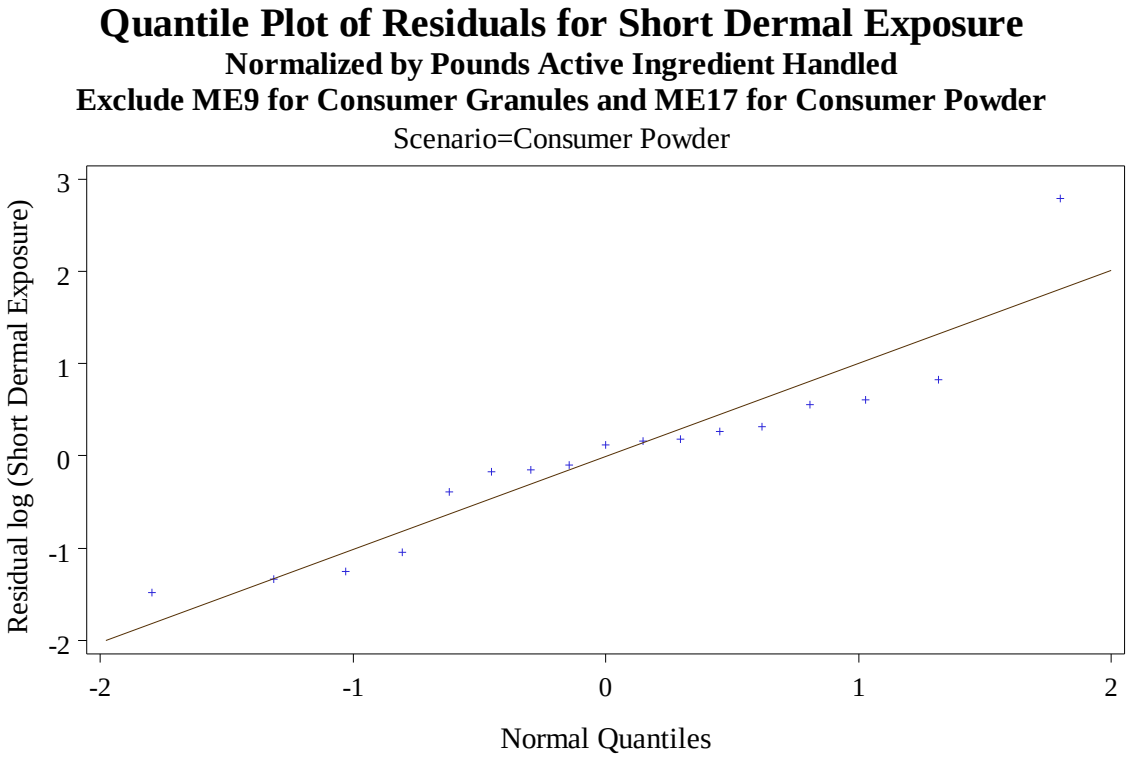

Figure 37. Quantile plot of residuals from linear model for Consumer Powder, Short Dermal, Exc. ME 17

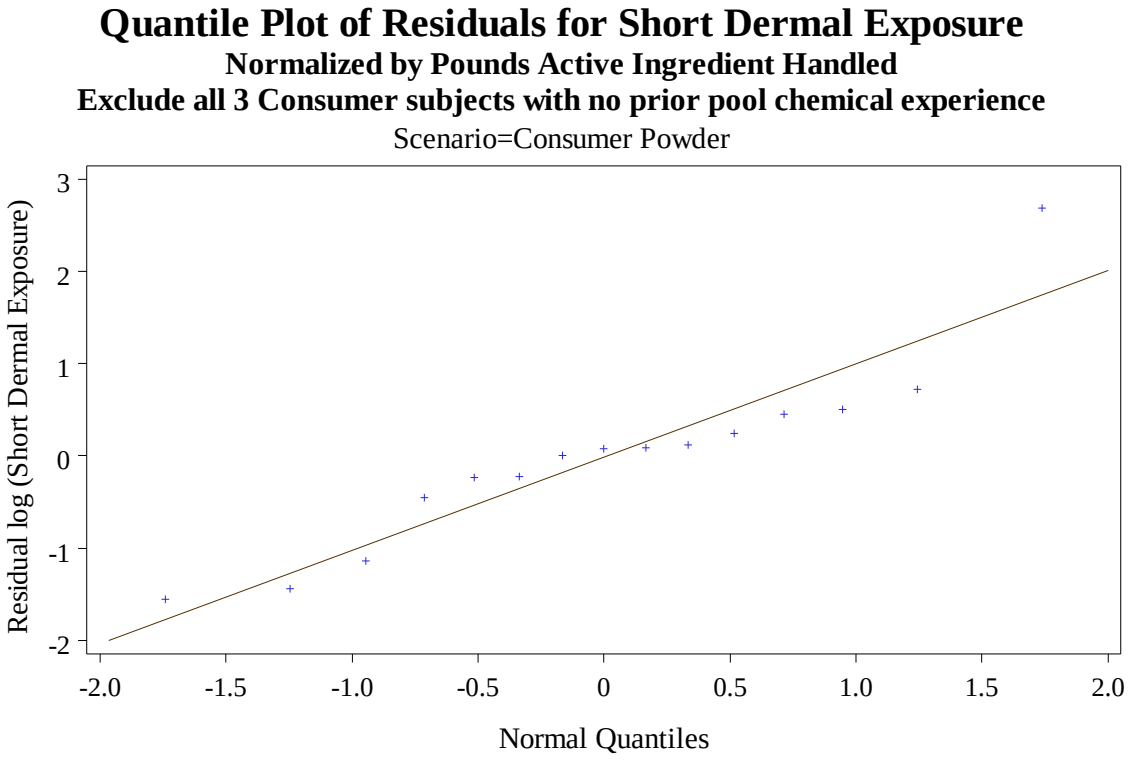

Figure 38. Quantile plot of residuals from linear model for Consumer Powder, Short Dermal, Experienced consumers

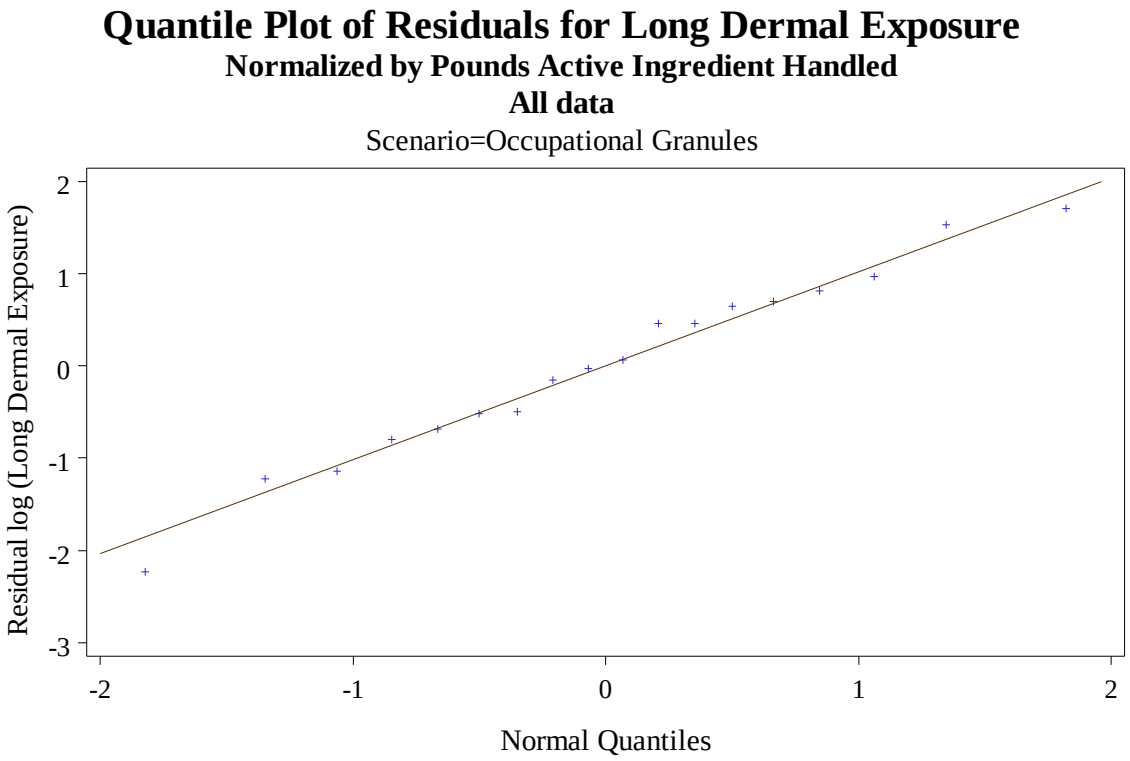

Figure 39. Quantile plot of residuals from linear model for Occupational Granules, Long Dermal, All data

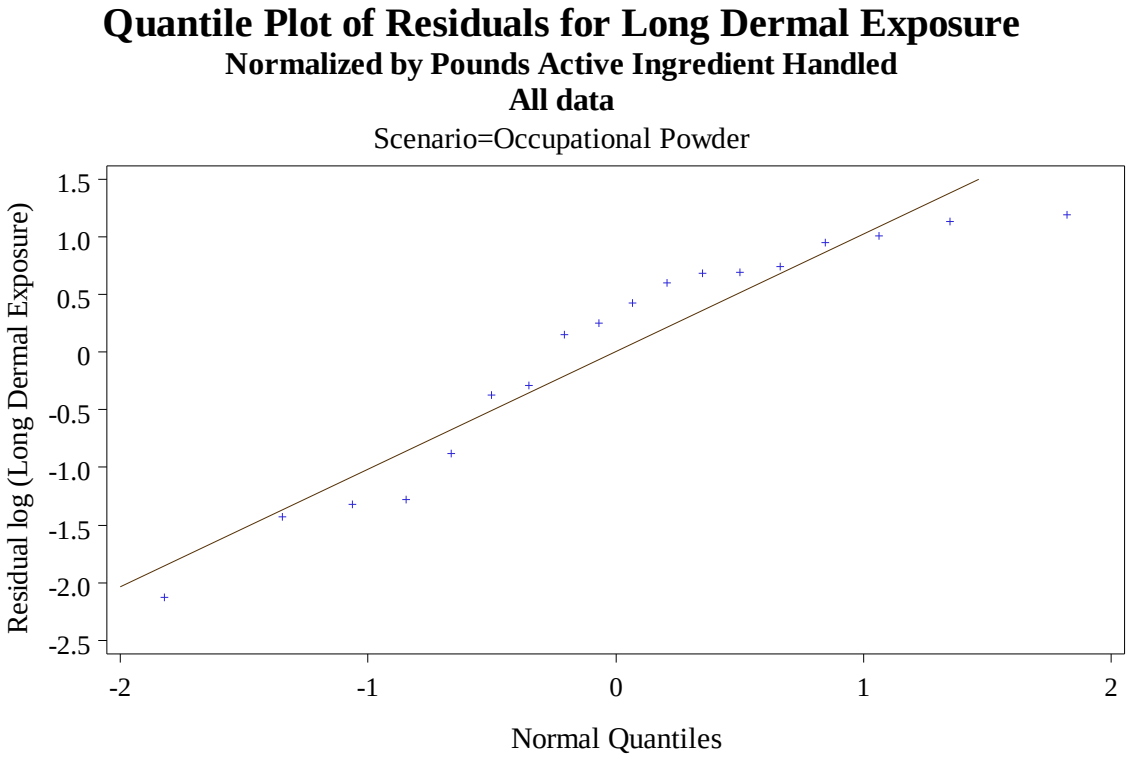

Figure 40. Quantile plot of residuals from linear model for Occupational Powder, Long Dermal, All data

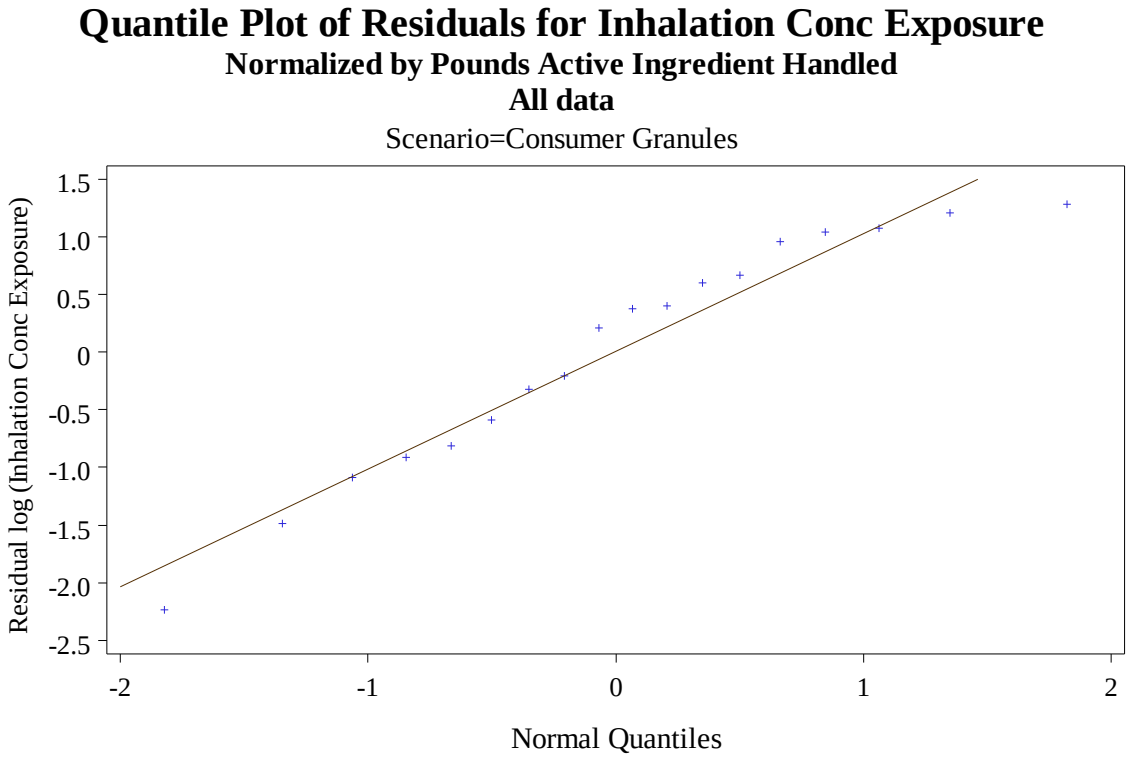

Figure 41. Quantile plot of residuals from linear model for Consumer Granules, Inhalation Concentration, All data

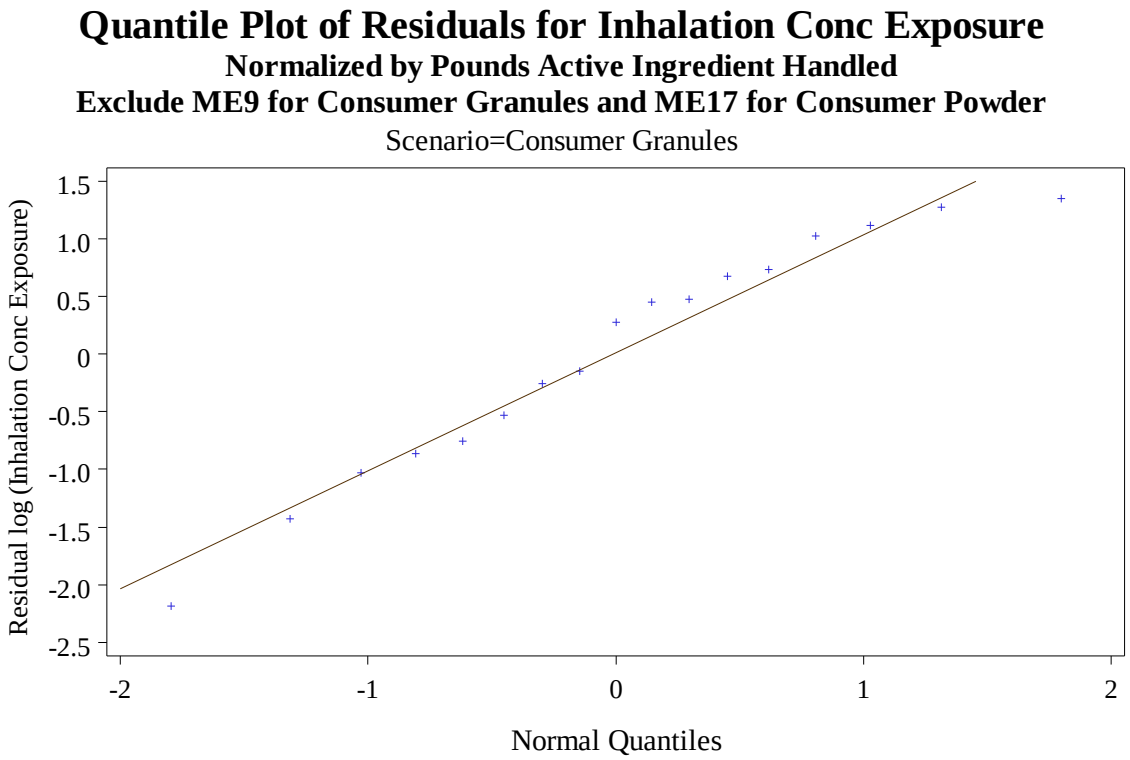

Figure 42. Quantile plot of residuals from linear model for Consumer Granules, Inhalation Concentration, Exc. ME 9

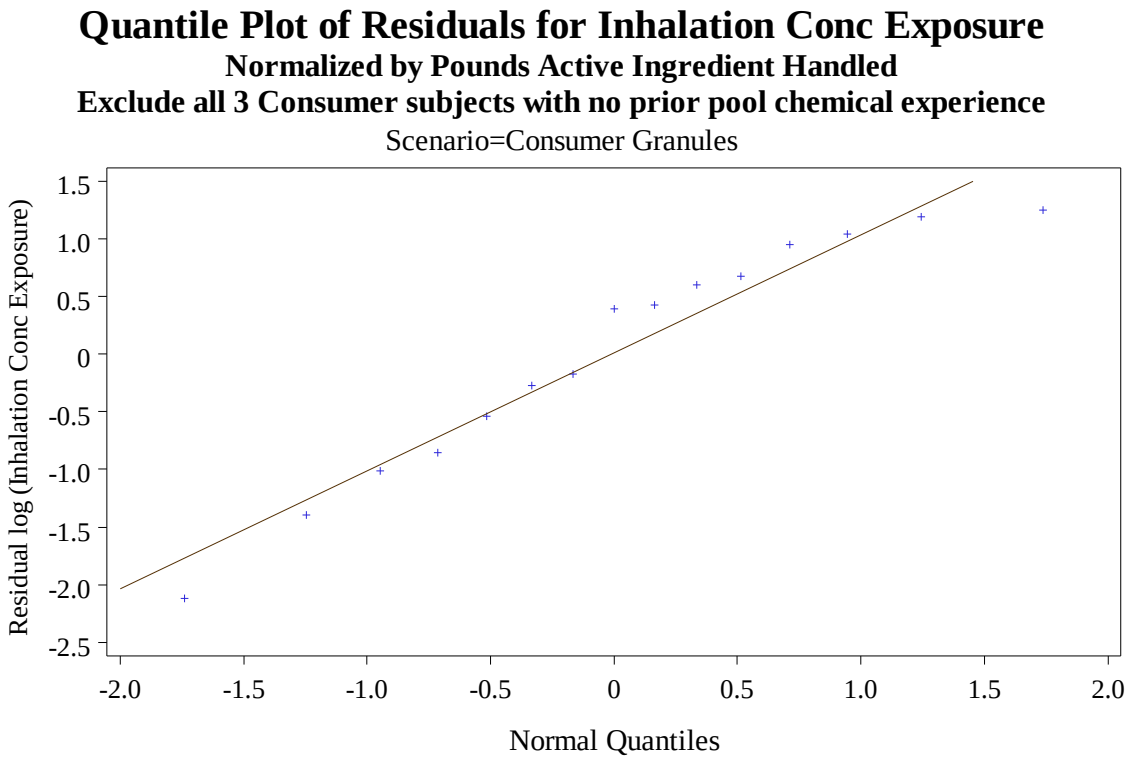

Figure 43. Quantile plot of residuals from linear model for Consumer Granules, Inhalation Concentration, Experienced consumers

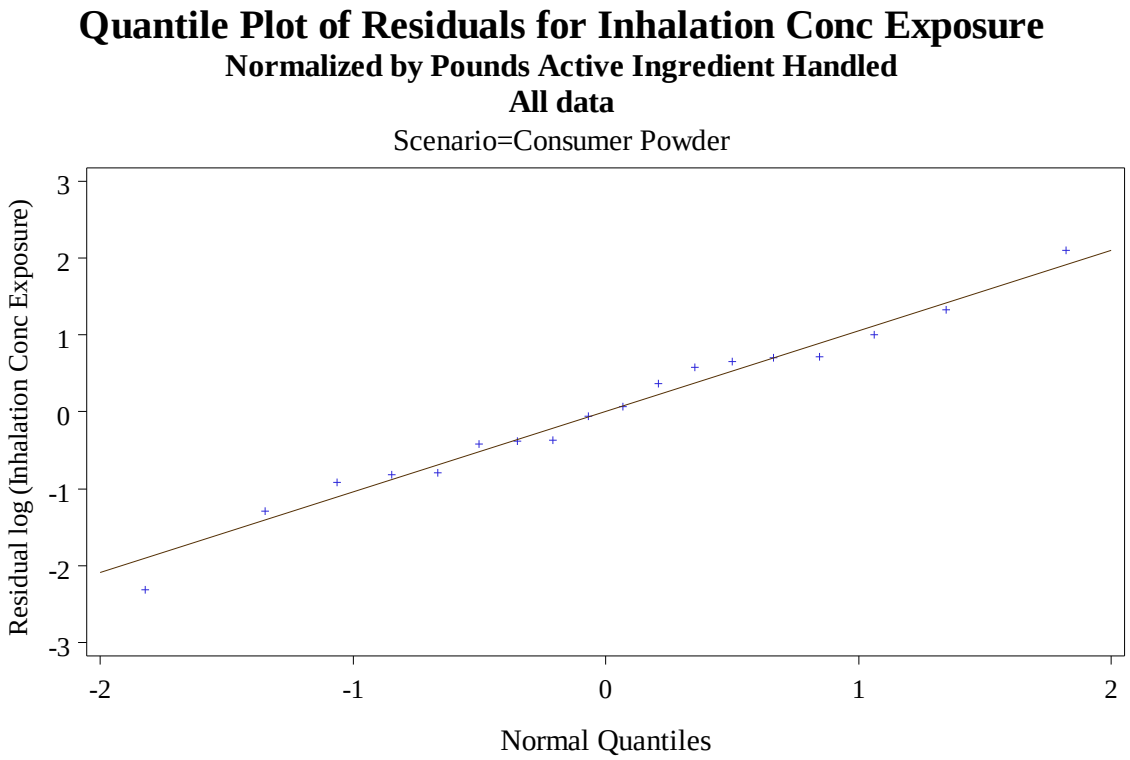

Figure 44. Quantile plot of residuals from linear model for Consumer Powder, Inhalation Concentration, All data

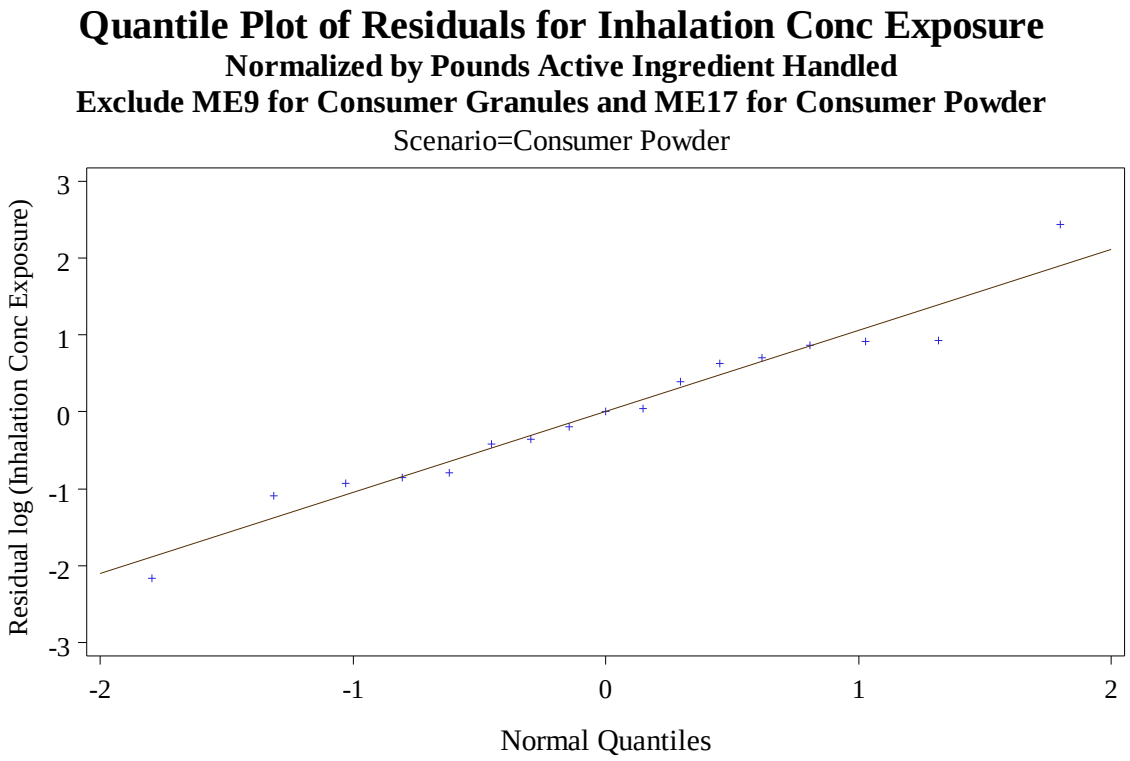

Figure 45. Quantile plot of residuals from linear model for Consumer Powder, Inhalation Concentration, Exc. ME 17

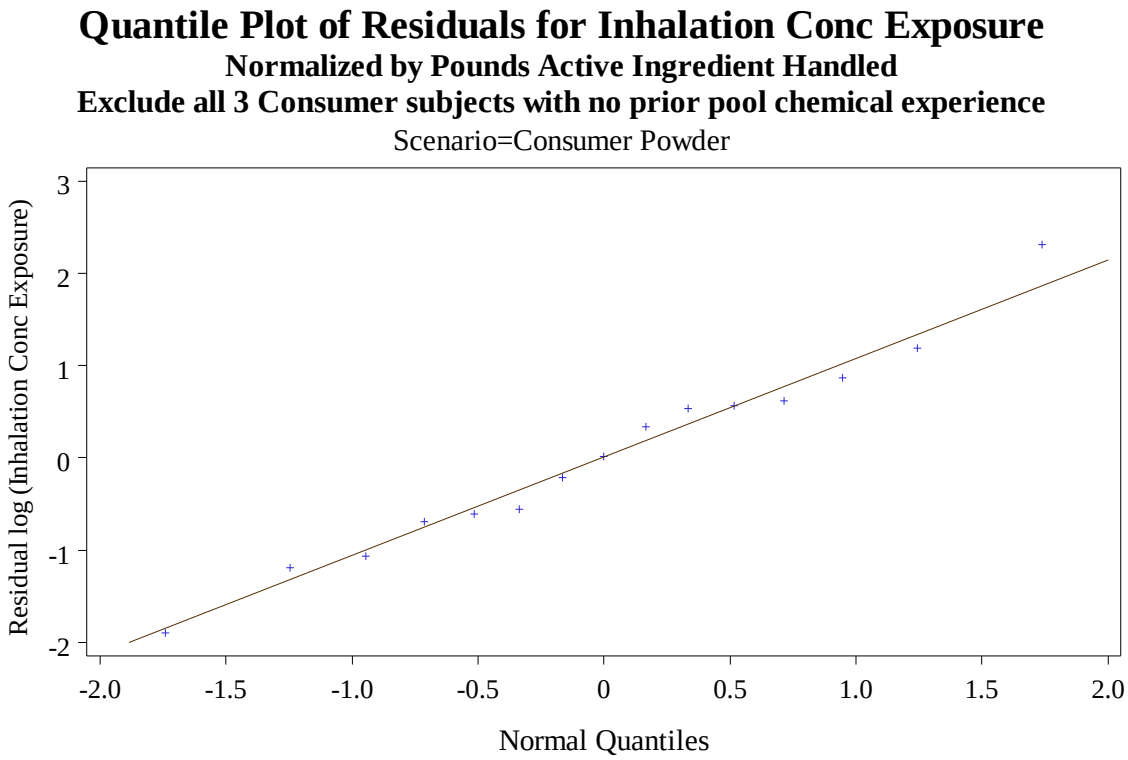

Figure 46. Quantile plot of residuals from linear model for Consumer Powder, Inhalation Concentration, Experienced consumers

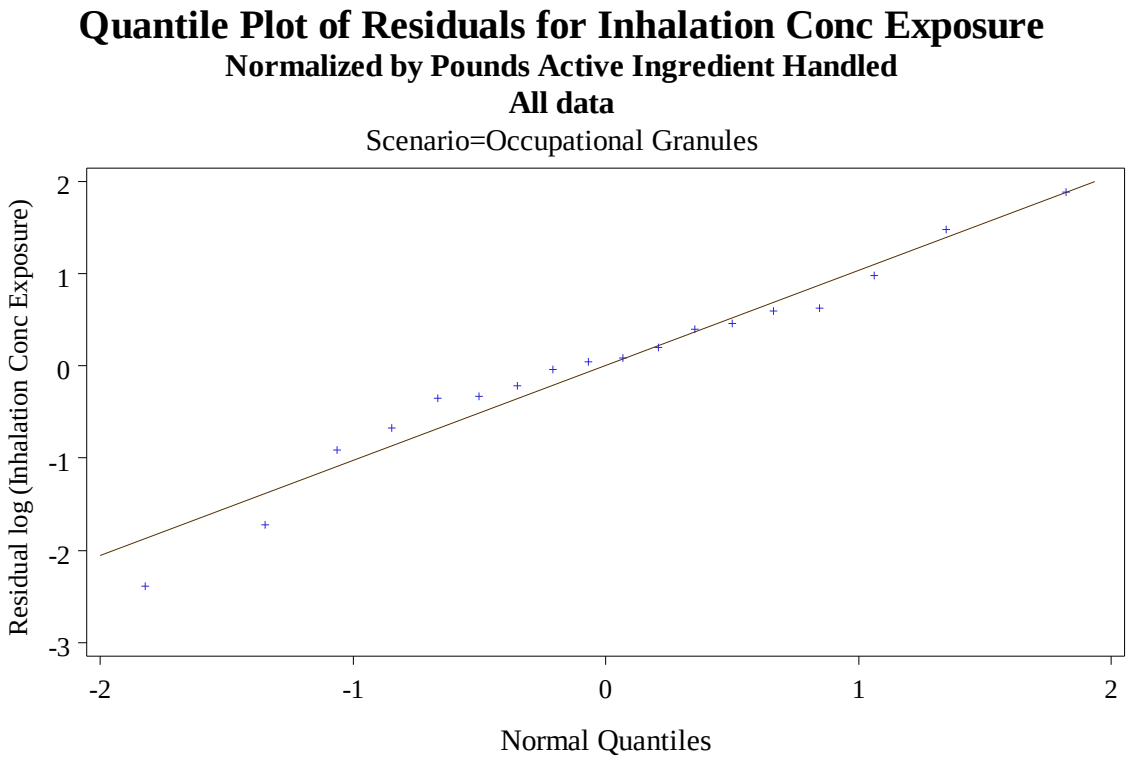

Figure 47. Quantile plot of residuals from linear model for Occupational Granules, Inhalation Concentration, All data

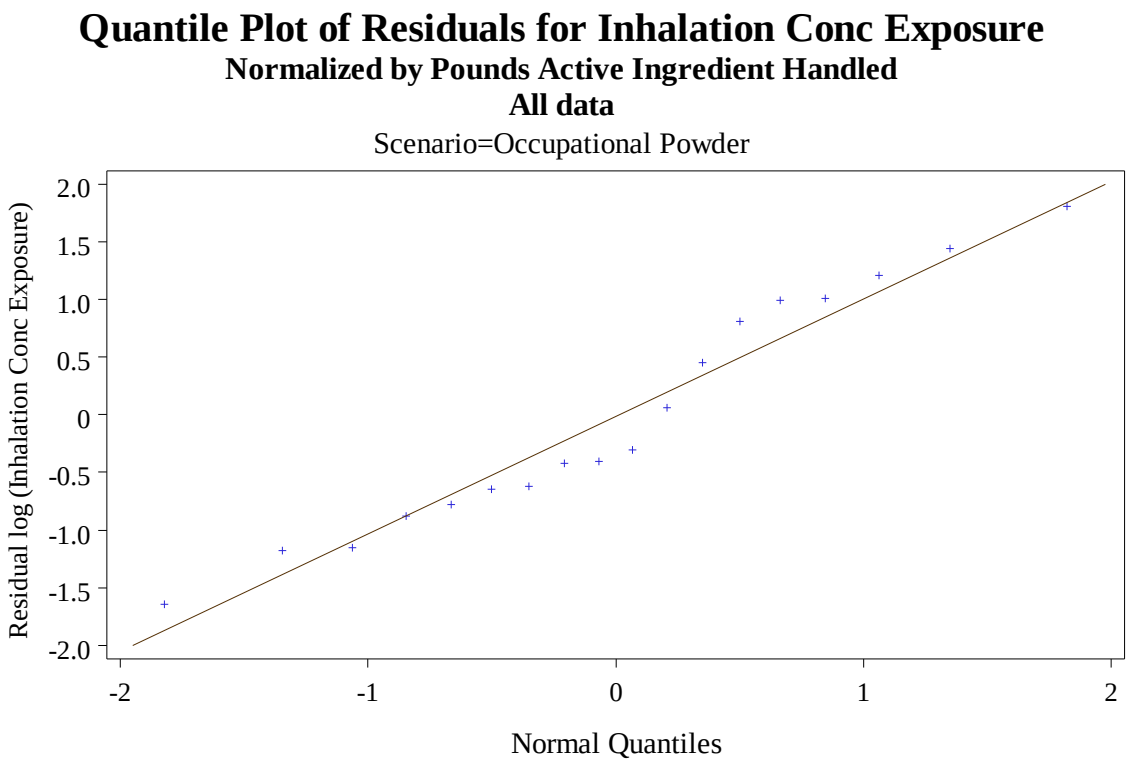

Figure 48. Quantile plot of residuals from linear model for Occupational Powder, Inhalation Concentration, All data

The quantile-quantile plots of the studentized residuals are reasonably close to the straight line but suggest that a more complicated model than a simple linear regression against the logarithm of the pounds of CYA used might fit the data even better. Interestingly, none of the studentized residuals exceeded the standard outlier cutoff of ±3, even for the Consumer models that included ME 9 (Consumer Granules) and ME 17 (Consumer Powder), the "outliers" identified in the study report. However, an outlier test based on the maximum unsigned studentized residual (with critical values computed by parametric bootstrap simulations) shows that for Consumer Granules, ME 9 is statistically significant at the 5% level, but not the 1% level, for the dermal exposure metrics. ME 17 for Consumer Powder was not found to be a statistically significant outlier at the 5% level.

Regression plots

The lognormal linear regression results for Short Dermal in the Consumer scenarios, Long Dermal in the Occupational scenarios, and Inhalation Concentration exposure for all four scenarios are shown in Figure 49 to Figure 64 using the half LOQ substitution method for non-detect values. Regression plots for the other exposure metrics are not included here but can be made available upon request. For Consumer Granules and Consumer Powder, the regression plots are shown for all the data, for the data excluding the potential outliers, and for the experienced consumers only. The scatter plots show the data points and the fitted regression lines. The data points marked with the symbol "E" are the experienced consumers or occupational workers (all the occupational workers were experienced). The data points marked with the symbol "O" are the two potential consumer outliers (ME 9 for Consumer Granules and ME 17 for Consumer Powder). The data points marked with the symbol "I" are the other two inexperienced consumers.

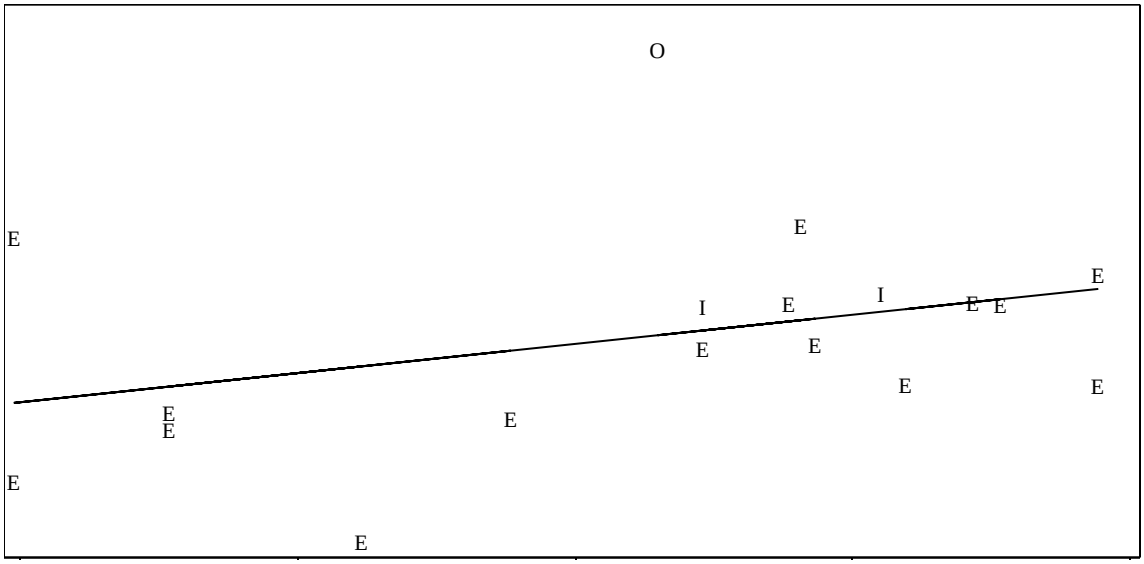

Figure 49. Regression plot for Consumer Granules, Short Dermal, All data

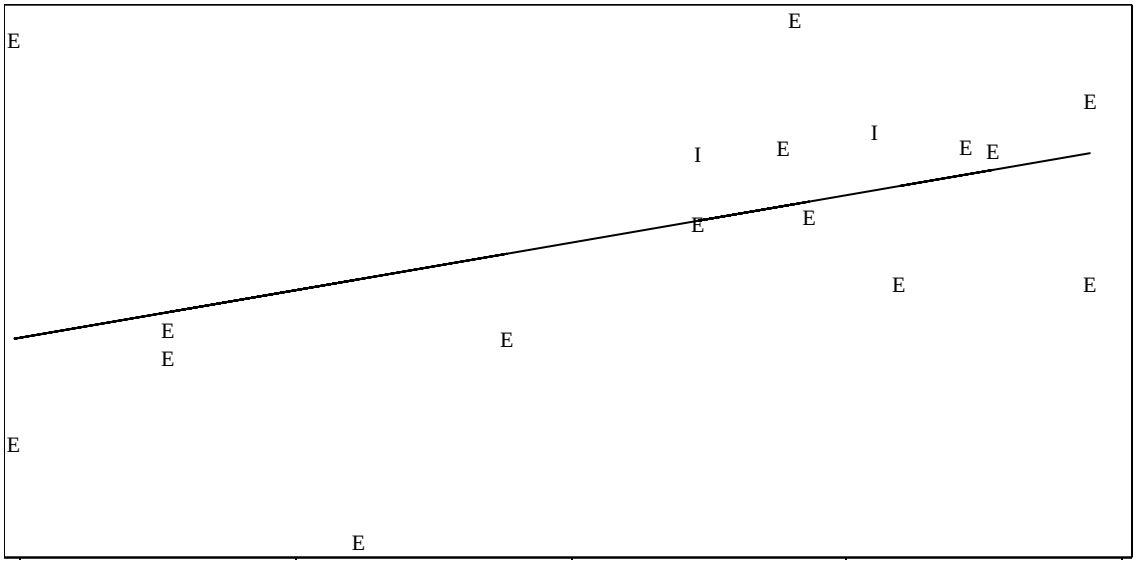

Figure 50. Regression plot for Consumer Granules, Short Dermal, Exc. ME 9

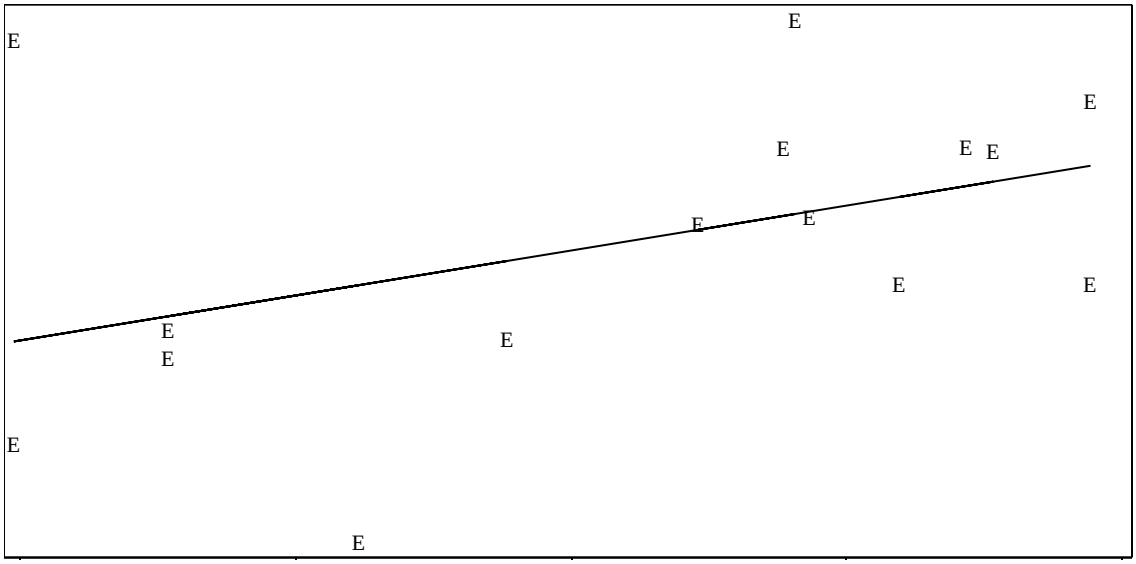

Figure 51. Regression plot for Consumer Granules, Short Dermal, Experienced consumers

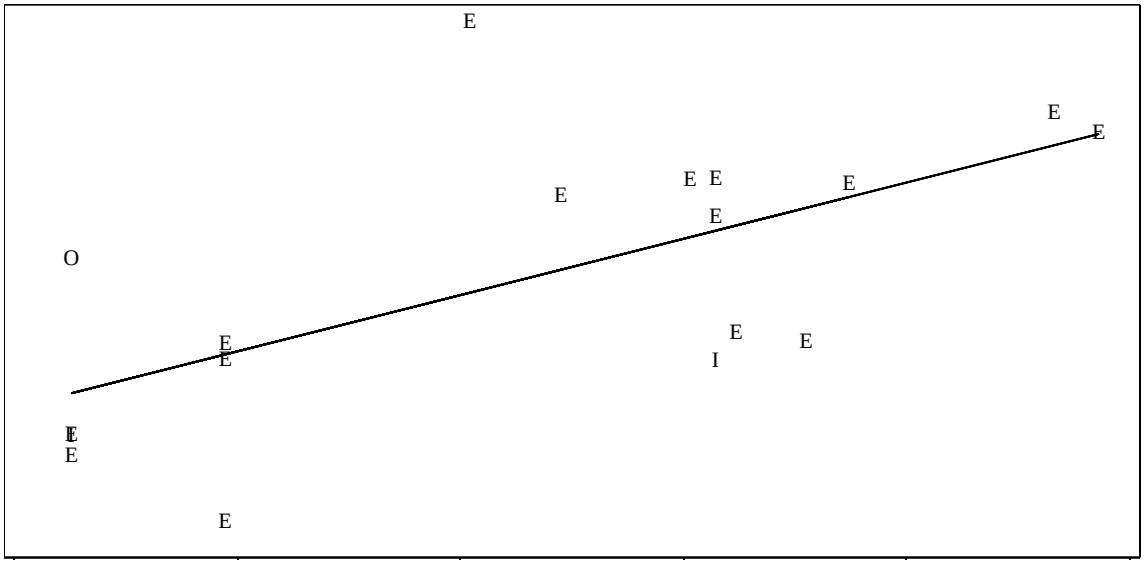

Figure 52. Regression plot for Consumer Powder, Short Dermal, All data

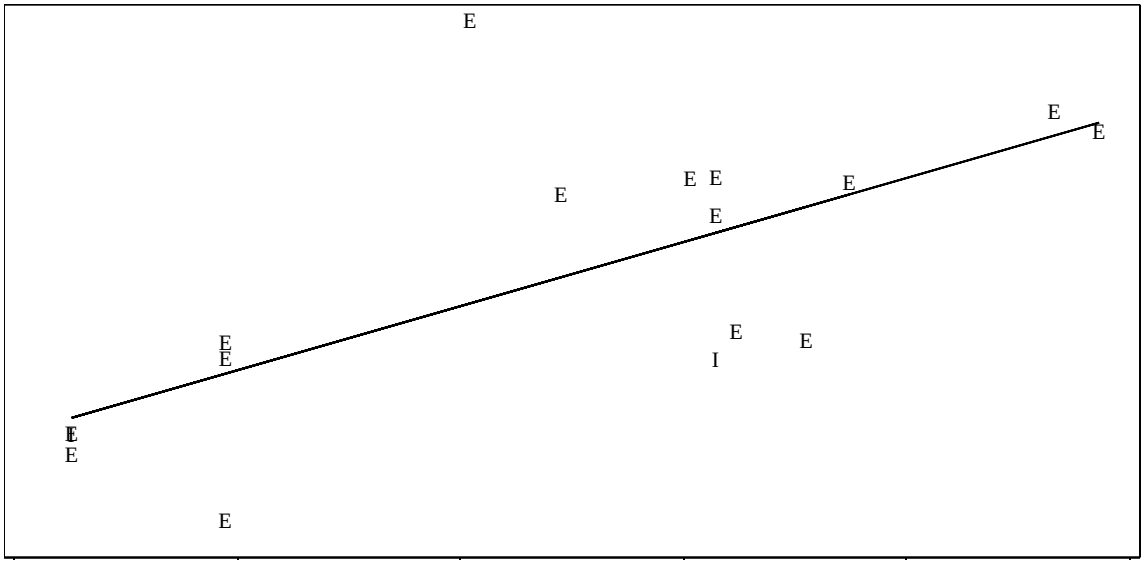

Figure 53. Regression plot for Consumer Powder, Short Dermal, Exc. ME 17

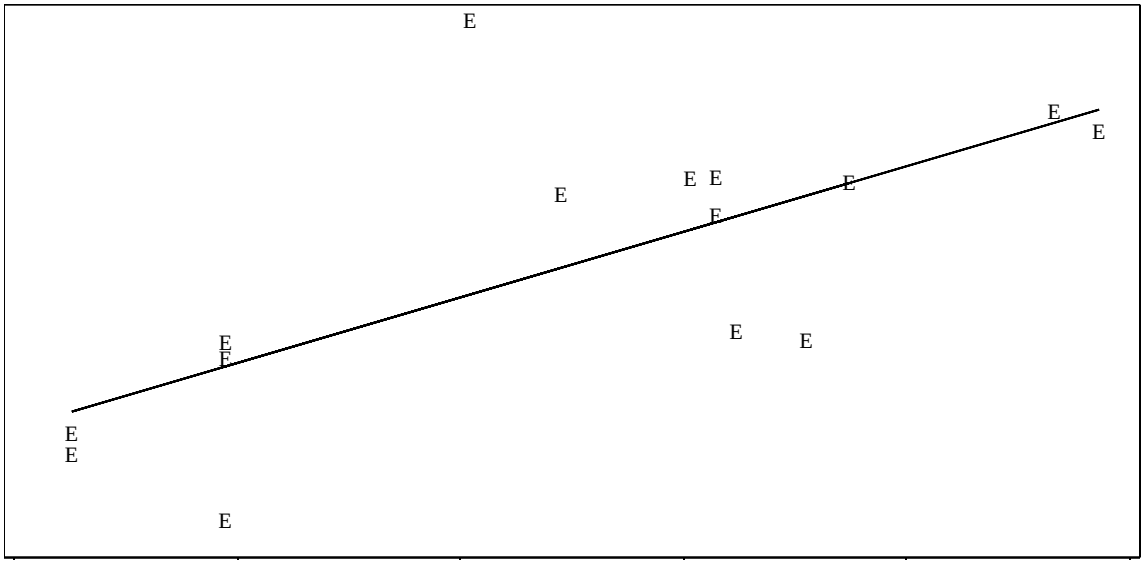

Figure 54. Regression plot for Consumer Powder, Short Dermal, Experienced consumers

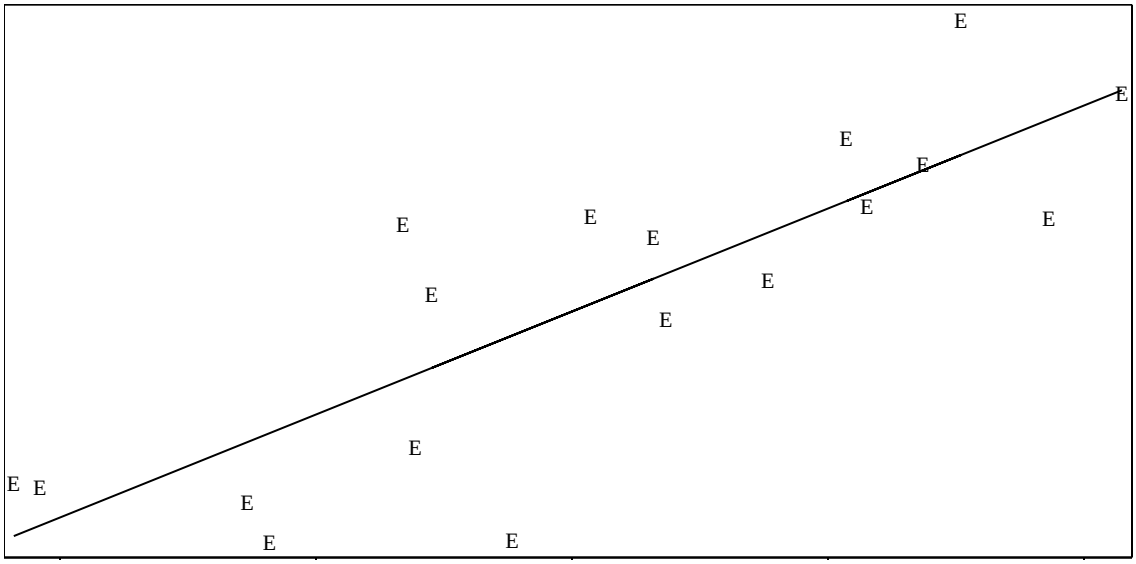

Figure 55. Regression plot for Occupational Granules, Long Dermal, All data

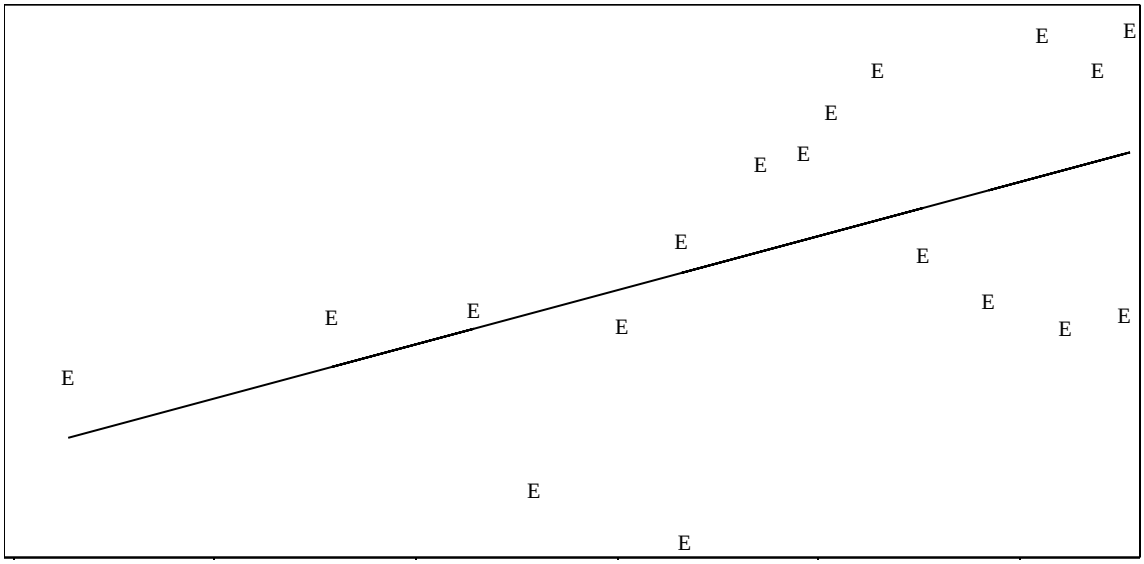

Figure 56. Regression plot for Occupational Powder, Long Dermal, All data

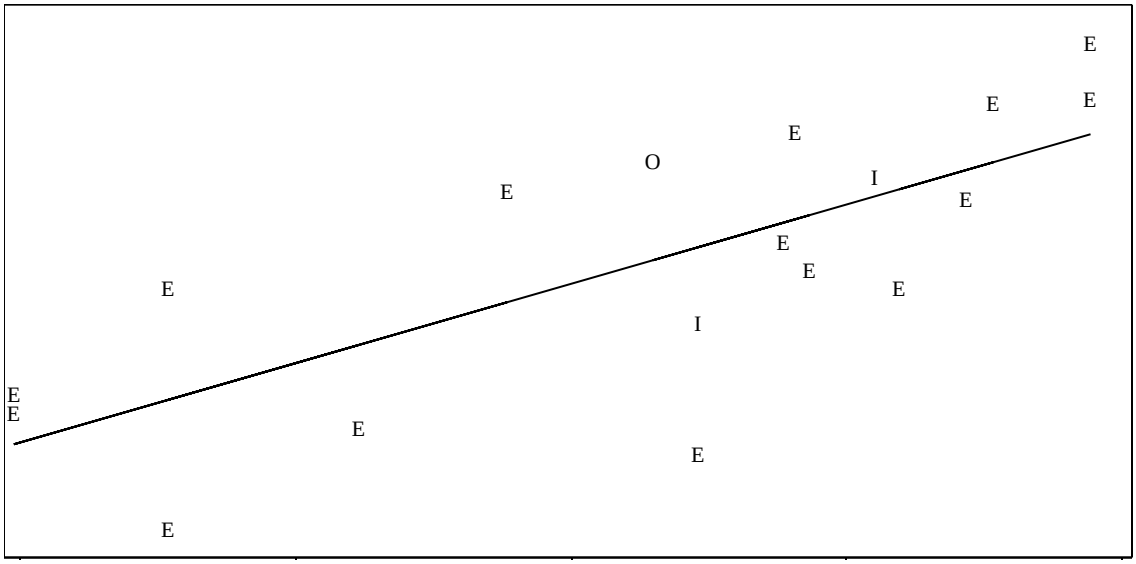

Figure 57. Regression plot for Consumer Granules, Inhalation Concentration, All data

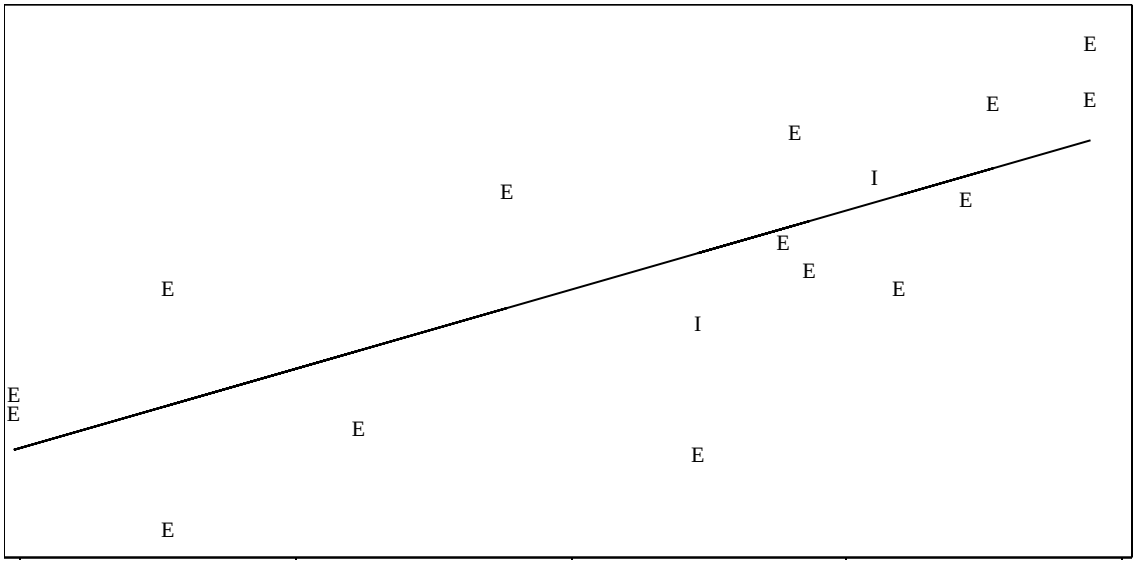

Figure 58. Regression plot for Consumer Granules, Inhalation Concentration, Exc. ME 9

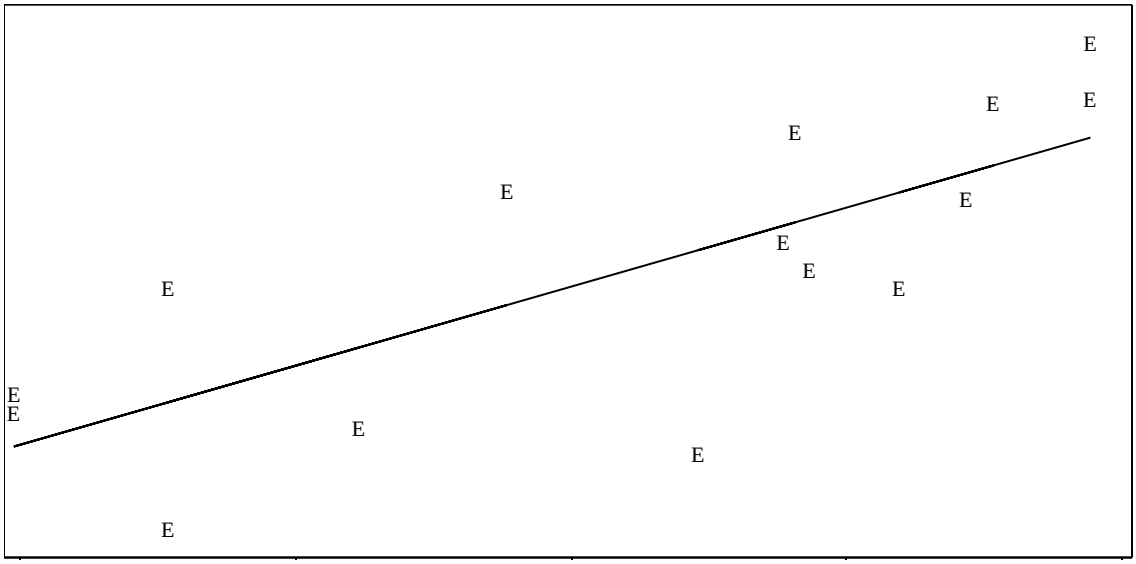

Figure 59. Regression plot for Consumer Granules, Inhalation Concentration, Experienced consumers

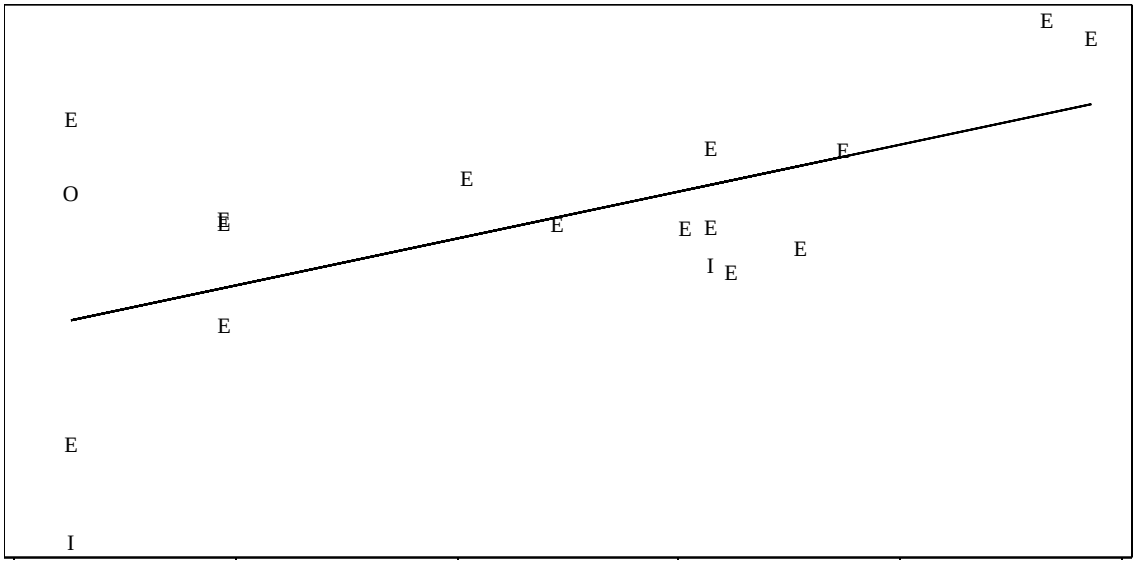

Figure 60. Regression plot for Consumer Powder, Inhalation Concentration, All data

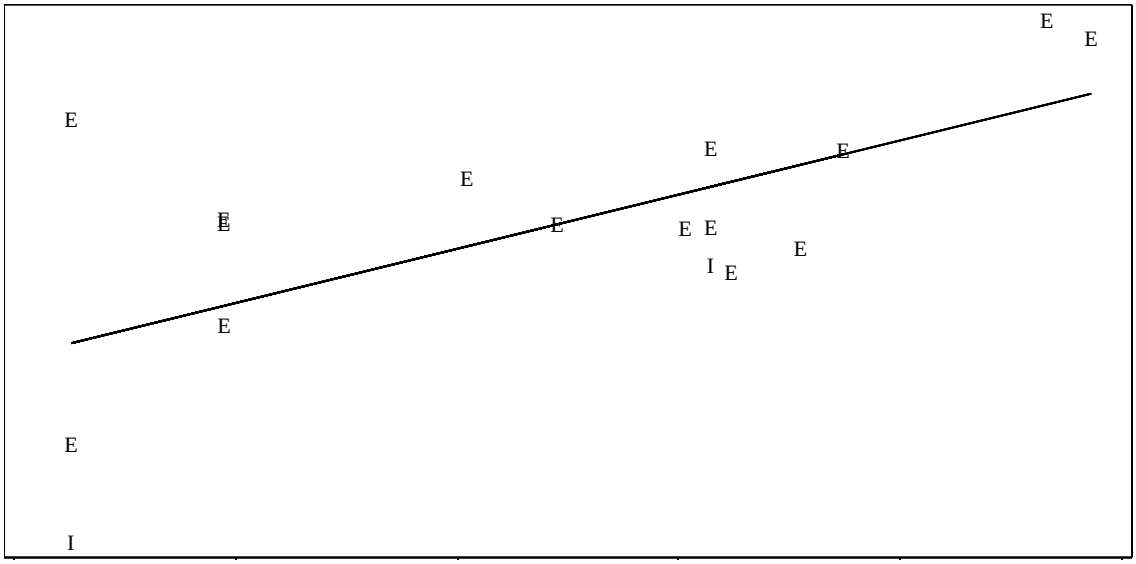

Figure 61. Regression plot for Consumer Powder, Inhalation Concentration, Exc. ME 17

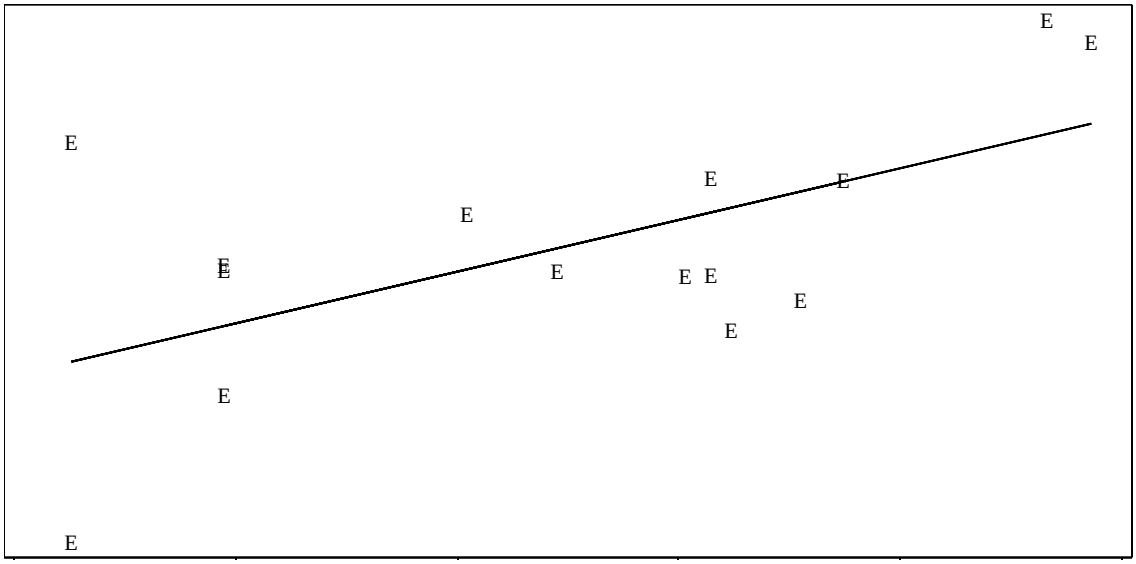

Figure 62. Regression plot for Consumer Powder, Inhalation Concentration, Experienced consumers

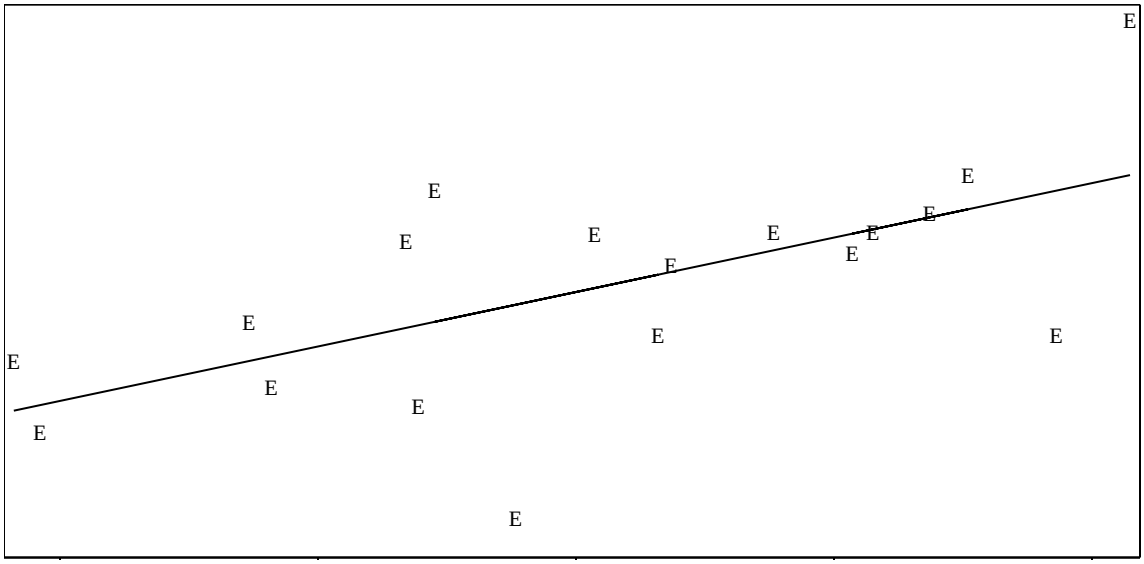

Figure 63. Regression plot for Occupational Granules, Inhalation Concentration, All data

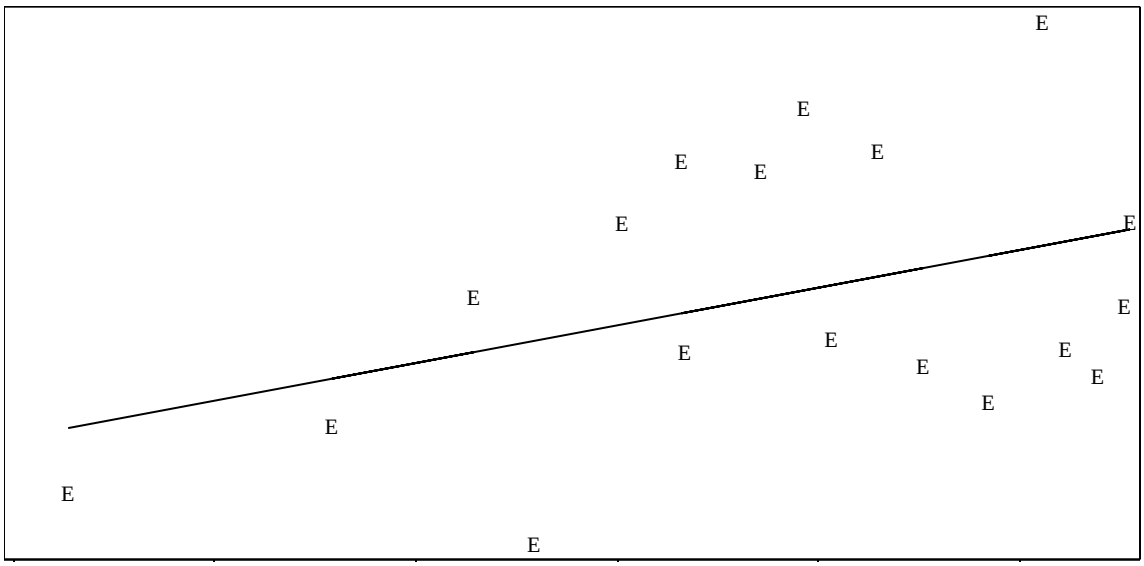

Figure 64. Regression plot for Occupational Powder, Inhalation Concentration, All data

The regression plots show the impacts on the Consumer scenarios of removing ME 9 for Granules and ME 17 for Powder, and then all the inexperienced consumers. For Consumer Granules, both for Short Dermal and Inhalation Concentration, the exposure values for ME 9 had values above the initial regression line as shown in Figure 49 and Figure 57. Since the amount of log(AI) was in the center of the distribution, removing ME 9 had little effect on the slope but reduced the intercept (as shown in Figure 50 and Figure 58). Also for Consumer Granules the other inexperienced consumers had exposure values quite close to the regression line and so their removal had little additional impact (as shown in Figure 51 and Figure 59). For Consumer Powder, both for Short Dermal and Inhalation Concentration, the exposure values for ME 17 had values above the initial regression line as shown in Figure 52 and Figure 60). Since the amount of log(AI) was in the center of the distribution, removing ME 17 had little effect on the slope but reduced the intercept (as shown in Figure 53 and Figure 61). For Consumer Powder Short Dermal, the other inexperienced consumers had exposure values quite close to the regression line and so their removal had little additional impact (Figure 56). For Consumer Powder Inhalation Concentration, one of the inexperienced consumers had a low log(AI) and exposure values much lower than the regression line and so their removal decreased the slope and increased the intercept (Figure 62).

9. Quadratic models

The log-log-linearity test was based on a linear model for log exposure versus log pounds active ingredient handled. The HSRB suggested that a quadratic model should also be considered.

There are two quadratic models that could be considered. Since the original linear model is of the form

Log (Exposure) = Intercept + Slope × Log (Pounds of Active Ingredient) + Error Terms,

the main quadratic model is of the form

Log (Exposure) = Intercept + Slope × Log (Pounds of Active Ingredient) + Quad × {Log (Pounds of Active Ingredient)}^{2}

+ Error Terms.

Note that the quadratic term is the square of the logarithm of the pounds of active ingredient rather than the logarithm of the square; the latter approach produces an ill-defined model with two multiples of the logarithm of the pounds of active ingredient.

Another approach might be to consider a quadratic model for exposure:

Exposure = Intercept + Slope × (Pounds of Active Ingredient) + Quad × (Pounds of Active Ingredient)^2
+ Error Terms.

We do not recommend this second approach for these data since the exposures are known to be non-negative and the quantile plots for hands only exposure data are better modeled using a log-normal distribution than using a normal distribution. Furthermore, unless the intercept is zero, this model predicts a nonzero exposure when the pounds of active ingredient is zero, and so a more realistic (though possibly poorer-fitting) model of this form would have a zero intercept. For other exposure data a log-log-linearity test could be carried out by fitting the zero intercept model

Exposure = Slope × (Pounds of Active Ingredient) + Quad × (Pounds of Active Ingredient)^2 + Error Terms

and testing if Quad equals zero.

The parsimony principle suggests that the appropriate statistical procedure for this study is to first fit the quadratic regression model for the logarithm of the exposure

Log (Exposure) = Intercept + Slope × Log (Pounds of Active Ingredient) +
Quad × {Log (Pounds of Active Ingredient)}^{2} + Error Terms.

If the coefficient Quad is statistically significant at the 5% level, which is equivalent to requiring that the 95% confidence interval does not include zero, than the quadratic model is supported. Otherwise the linear model should be used.

Table 41 presents the quadratic coefficient Quad from the fitted quadratic regression models for Short Dermal in the Consumer scenarios, Long Dermal in the Occupational scenarios, and Inhalation Concentration exposure for all four scenarios are shown in Figure 49 to Figure 64 using the half LOQ substitution method for non-detect values. Intercepts, slopes, and results for the other exposure metrics are not included here but can be made available upon request. These calculations use the half LOQ substitution method for non-detects.

Table 41. Quadratic coefficients with 95% confidence intervals for quadratic regression models for the log exposure versus log pounds active ingredient handled

Scenario	Exposure Route	Data	Estimate	Lower Bound	Upper Bound
Consumer Granules	Short Dermal	All	-0.098	-0.673	0.478
		Excl. ME 9	0.117	-0.331	0.565
		Experienced	0.171	-0.328	0.670
	Inhalation Concentration	All	0.183	-0.155	0.522
		Excl. ME 9	0.252	-0.088	0.592
		Experienced	0.241	-0.146	0.628
Consumer Powder	Short Dermal	All	-0.056	-0.357	0.245
		Excl. ME 9	-0.106	-0.404	0.193
		Experienced	-0.150	-0.473	0.172
	Inhalation Concentration	All	0.120	-0.159	0.399
		Excl. ME 9	0.252	-0.088	0.592
		Experienced	0.164	-0.087	0.415
Occupational Granules	Long Dermal	All	0.127	-0.697	0.951
	Inhalation Concentration	All	0.428	-0.843	1.699
Occupational Powder	Long Dermal	All	0.163	-0.551	0.877
	Inhalation Concentration	All	-0.382	-1.003	0.238

Since the 95% confidence intervals for Quad include zero in every case, the quadratic coefficient is not statistically significant and the quadratic models are not supported.

10. Threshold Analyses

As shown above, two statistical models were fitted to the dermal and inhalation exposure data and can be used to estimate the conditional mean exposure, i.e., the expected exposure conditional on the amount of active ingredient, E{Exposure | AI}.

Linear Model

$$\text{Log (Exposure)} = \text{Intercept} + \text{Slope} \times \text{Log (Pounds of Active Ingredient)} + \text{Random Error},$$

which implies

Equation 1: E{Exposure | AI} = Expected Exposure Given the Pounds of Active Ingredient = $C \times AI^{Slope}$,

where

$C = e^{Intercept} \times e^{Varerror/2}$.

Lognormal Model

If the value of Slope in the linear model is 1, then

Log (Normalized Exposure) = Log(Exposure / Pounds of Active Ingredient)

= Intercept* + Random Error,

which implies

Equation 2: E{Exposure | AI} = Expected Exposure Given the Pounds of Active Ingredient = $C^* \times AI$,

where

$C^* = e^{Intercept^*} \times e^{Varerror^*/2}$.

(The parameters for the lognormal model are asterisked). If Slope equals 1 then the two models are identical.

These two statistical models can be compared by calculating the threshold value of the pounds of active ingredient at which both models predict the same conditional mean exposure.

Define Threshold = $\left(\frac{C}{C^*}\right)^{\frac{1}{1-Slope}}$.

Thus E(X | AI) for the lognormal model > E(X | AI) for the linear model if and only if

$C^* \times AI > C \times AI^{Slope}$, which is true if and only if

Either Slope < 1 and AI > Threshold

Or Slope > 1 and AI < Threshold.

These are the conditions under which the lognormal model overestimates exposure compared to the linear model.

The most useful case is when slope < 1. If so, the lognormal model is “more conservative” (i.e., predicts higher exposure) when the pounds of active ingredient is high (more specifically, above the threshold). When the pounds of active ingredient is below the threshold, then either the linear model equation $C \times AI^{Slope}$ can be used to estimate the conditional mean exposure, or instead one can use the upper bound C* × Threshold. If AI = Threshold, then the estimates of the conditional mean exposure are the same.

The Threshold pounds of AI values and corresponding exposure values C* × Threshold were tabulated together with the estimated slopes in Table 37 to Table 40 above.

We now have two estimates of the conditional mean exposure for a given amount of active ingredient, equations 1 and 2. The graphs in Figure 65 to Figure 80 below compare the conditional mean exposure estimates for Short Dermal in the Consumer scenarios, Long Dermal in the Occupational scenarios, and Inhalation Concentration exposure for all four scenarios. The conditional mean exposure is plotted against the pounds of active ingredient. The brown curve gives the estimates for the linear model in equation 1. The green line gives the estimates for the lognormal model in equation 2. The two estimates are equal if the pounds of active ingredient equals the Threshold value. The data points marked with the symbol "E" are the experienced consumers or occupational workers (all the occupational workers were experienced). The data points marked with the symbol "O" are the two potential consumer outliers (ME 9 for Consumer Granules and ME 17 for Consumer Powder). The data points marked with the symbol "I" are the other two inexperienced consumers.

For all the cases for Consumer Granules and Powder, and some of the cases for Occupational Granules and Powder the estimated slope is less than 1. As proven above, the conditional mean exposure from the lognormal model will be greater than the conditional mean exposure from the linear model for amounts of active ingredient above the threshold (right hand side of the graph). The conditional mean exposure from the lognormal model will be less than the conditional mean exposure from the linear model for amounts of active ingredient below the threshold (left hand side of the graph).

For some of the cases for Occupational Granules and Powder the estimated slope is greater than 1. As proven above, the conditional mean exposure from the lognormal model will be less than the conditional mean exposure from the linear model for amounts of active ingredient above the threshold (right hand side of the graph). The conditional mean exposure from the lognormal model will be greater than the conditional mean exposure from the linear model for amounts of active ingredient below the threshold (left hand side of the graph).

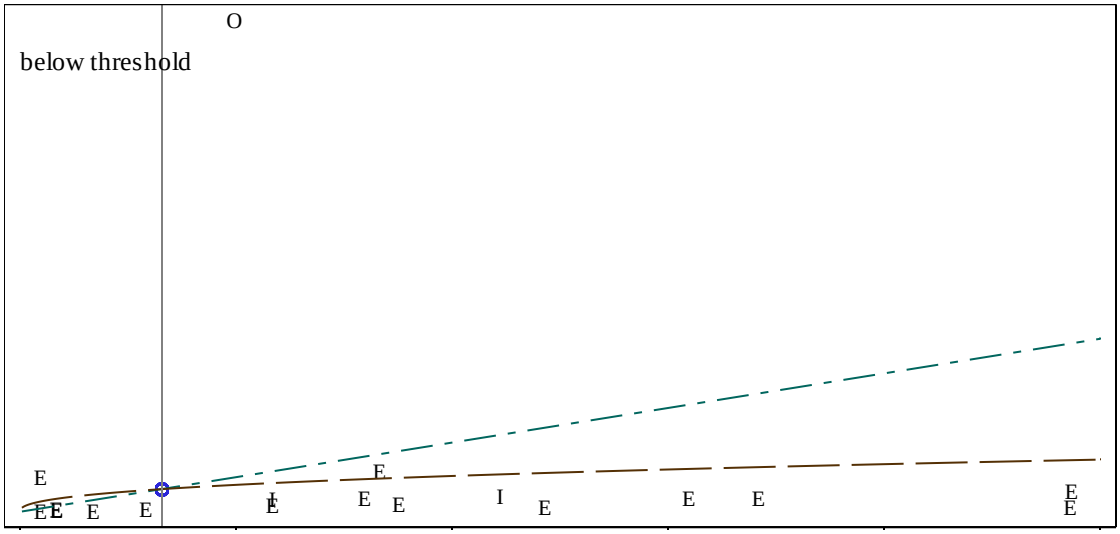

Figure 65. Threshold plot for Consumer Granules, Short Dermal, All data

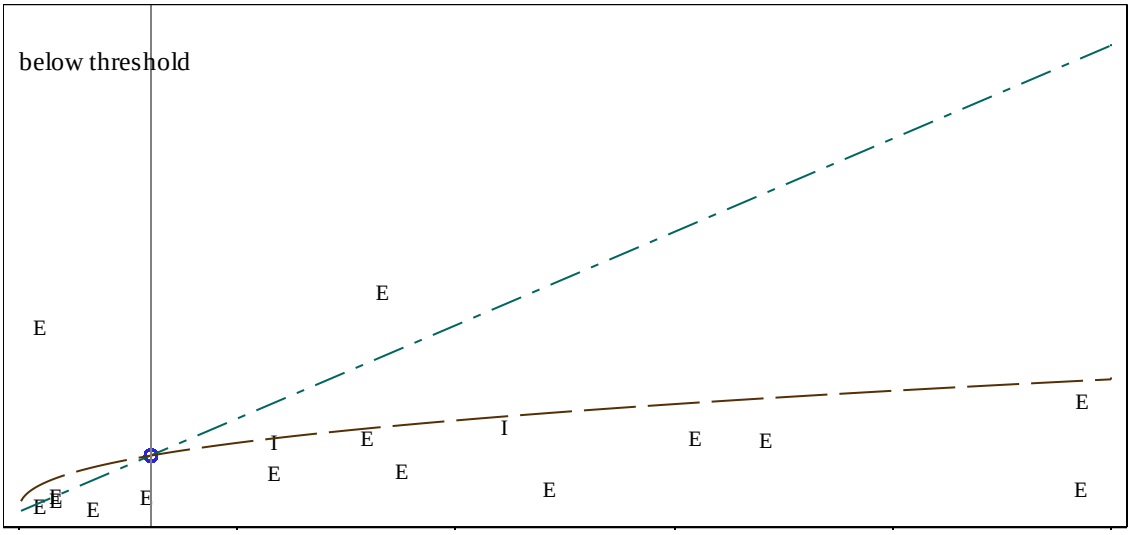

Figure 66. Threshold plot for Consumer Granules, Short Dermal, Exc. ME 9

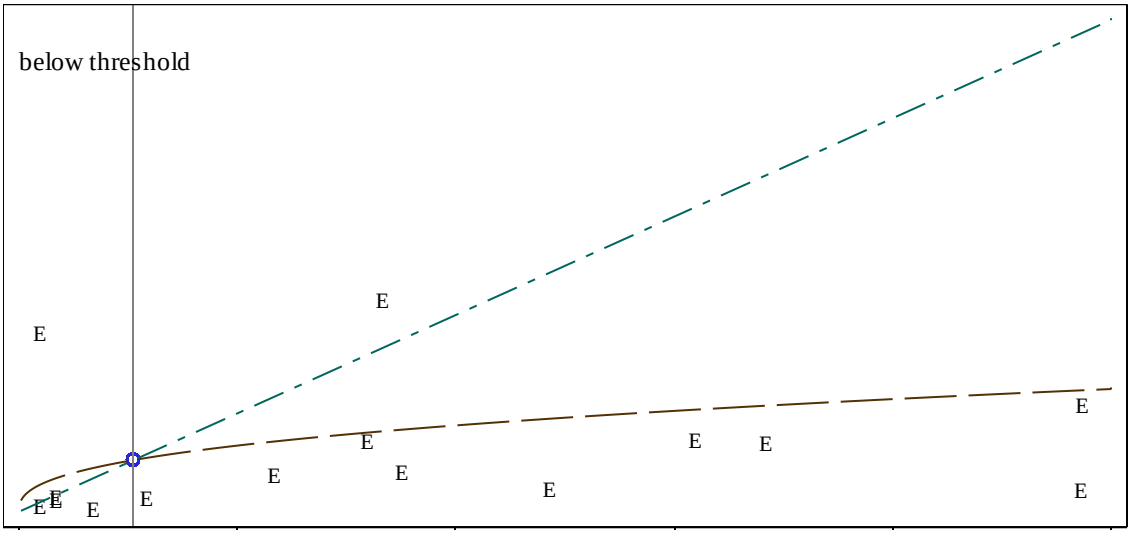

Figure 67. Threshold plot for Consumer Granules, Short Dermal, Experienced consumers

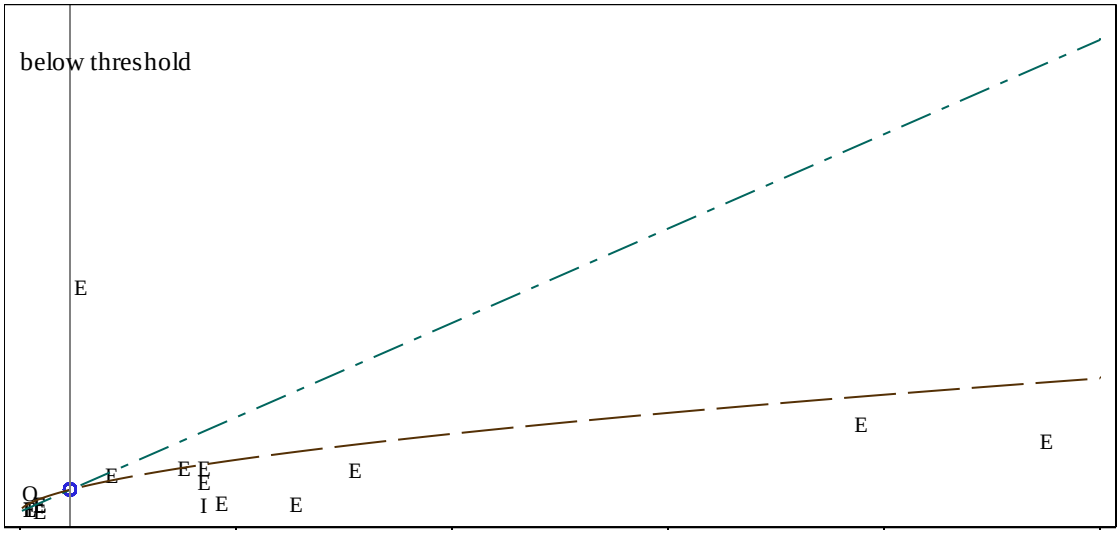

Figure 68. Threshold plot for Consumer Powder, Short Dermal, All data

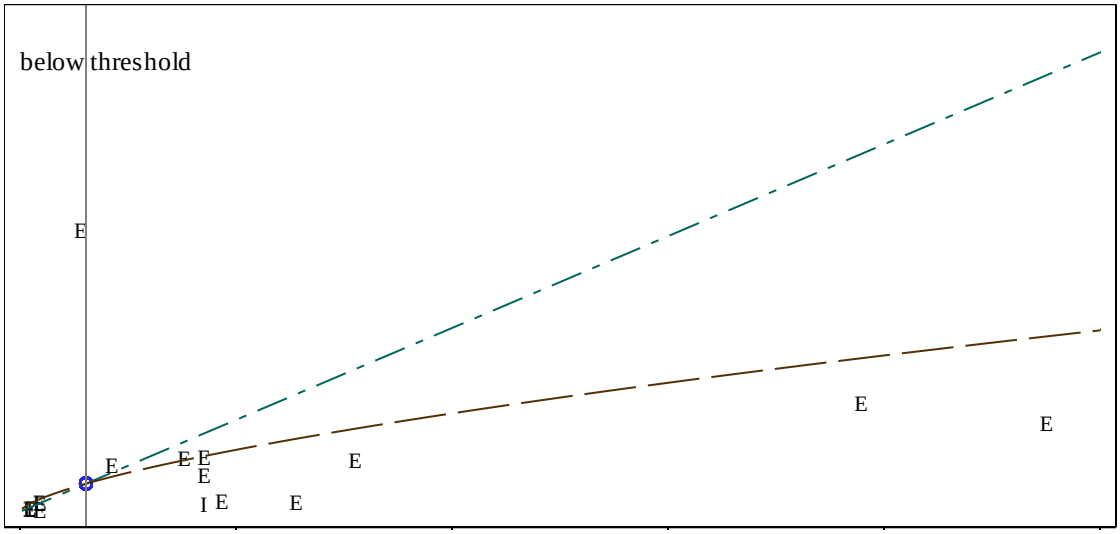

Figure 69. Threshold plot for Consumer Powder, Short Dermal, Excl ME 17

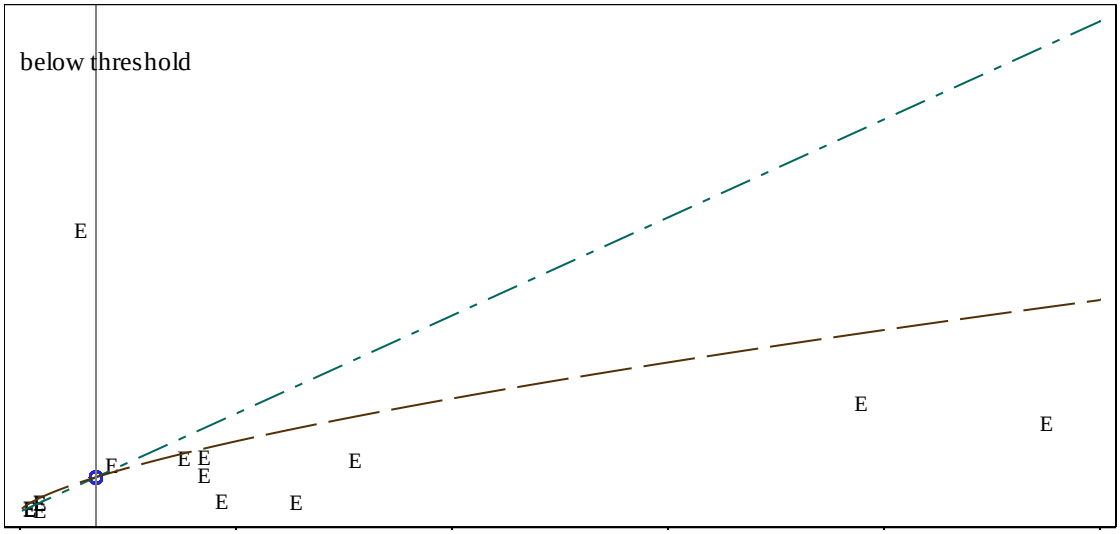

Figure 70. Threshold plot for Consumer Powder, Short Dermal, Experienced consumers

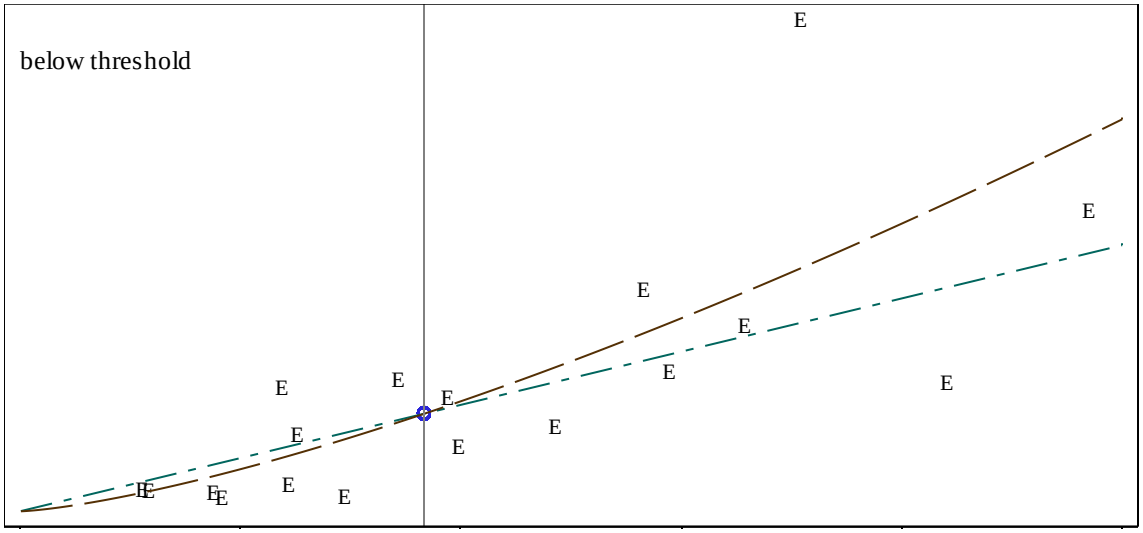

Figure 71. Threshold plot for Occupational Granules, Long Dermal, All data

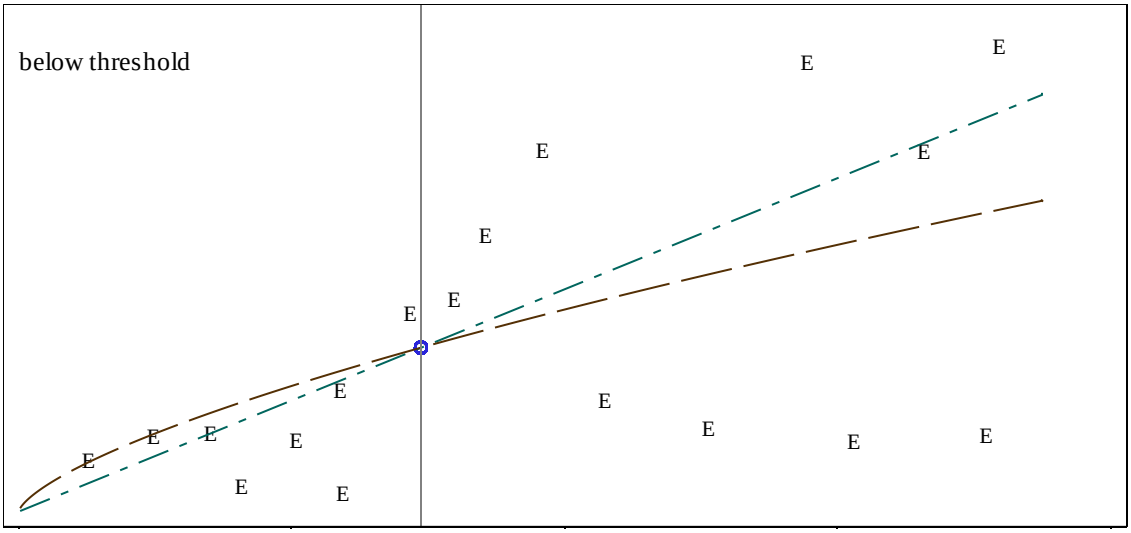

Figure 72. Threshold plot for Occupational Powder, Long Dermal, All data

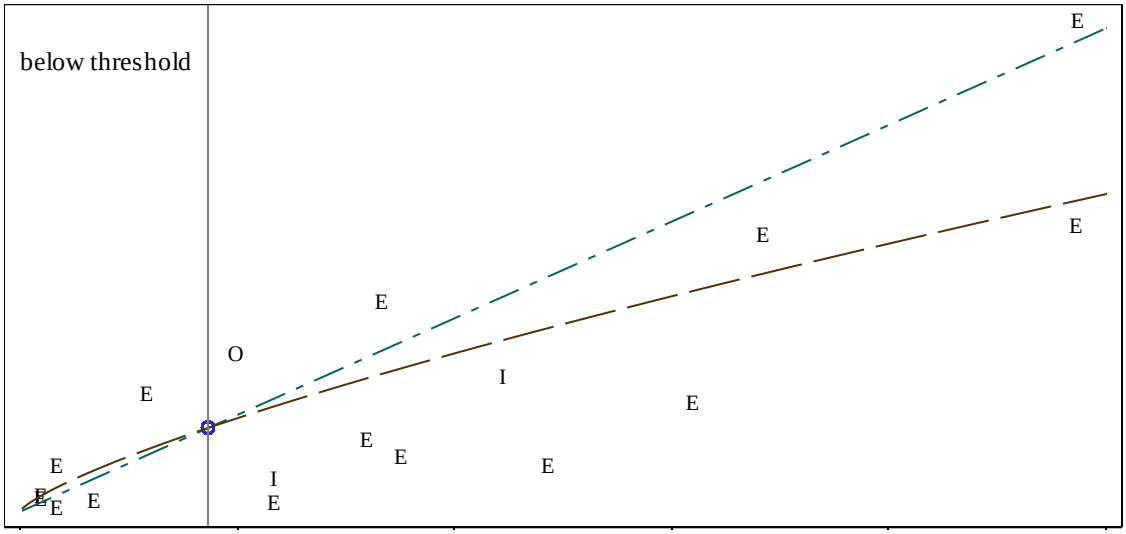

Figure 73. Threshold plot for Consumer Granules, Inhalation Concentration, All data

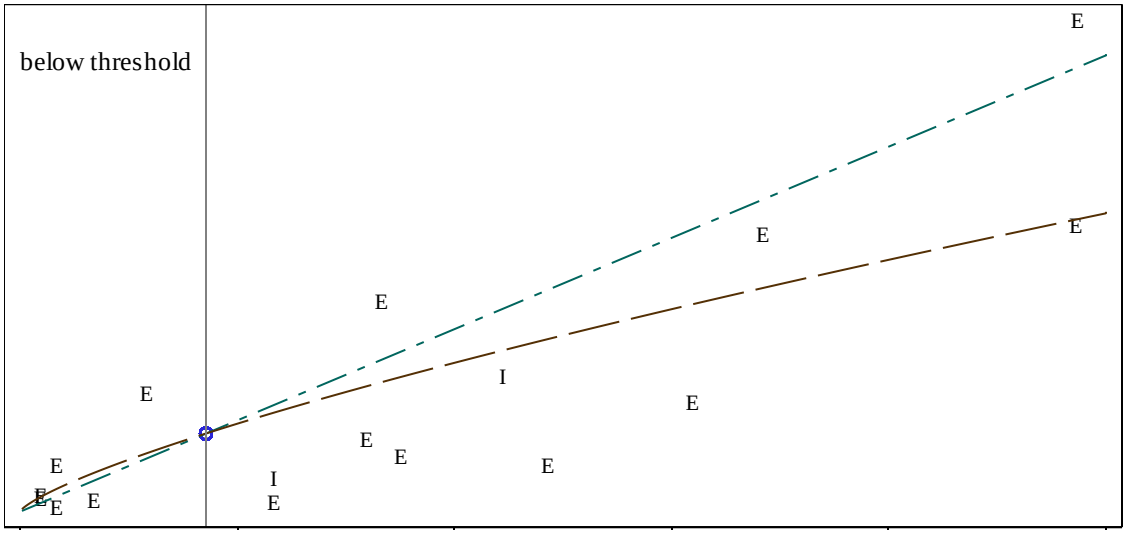

Figure 74. Threshold plot for Consumer Granules, Inhalation Concentration, Exc. ME 9

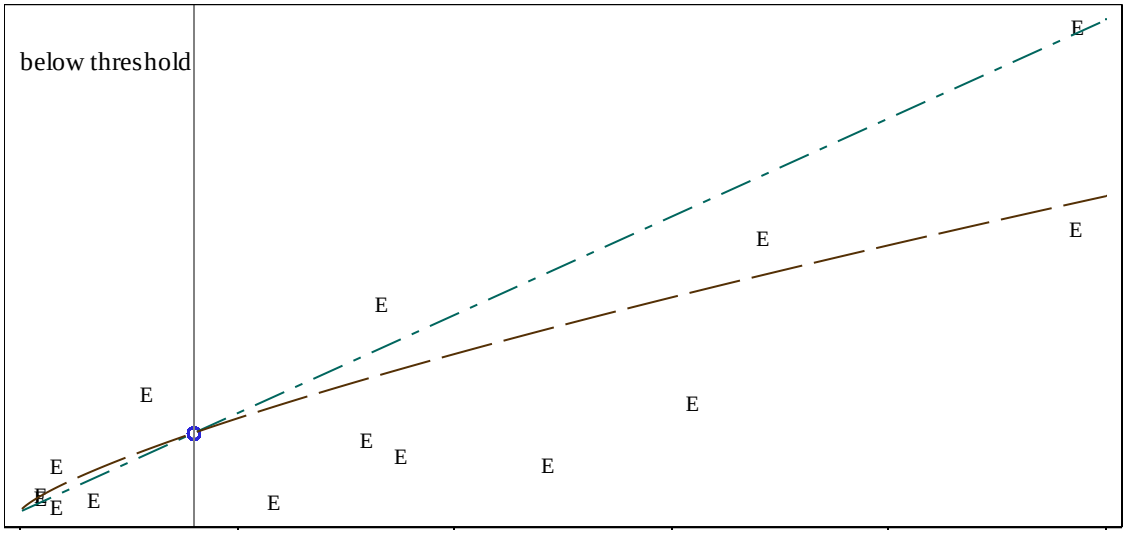

Figure 75. Threshold plot for Consumer Granules, Inhalation Concentration, Experienced consumers

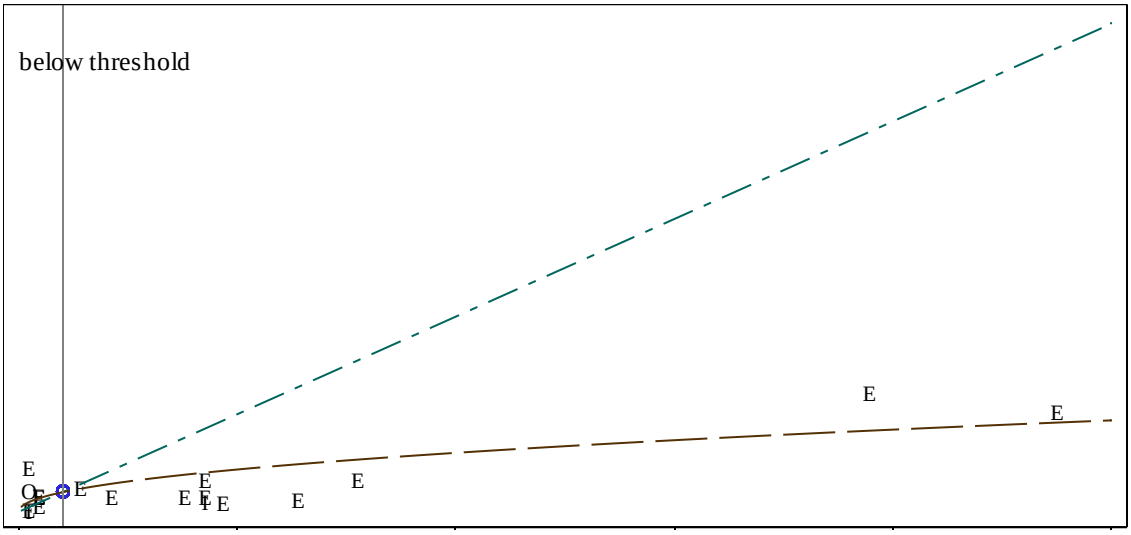

Figure 76. Threshold plot for Consumer Powder, Inhalation Concentration, All data

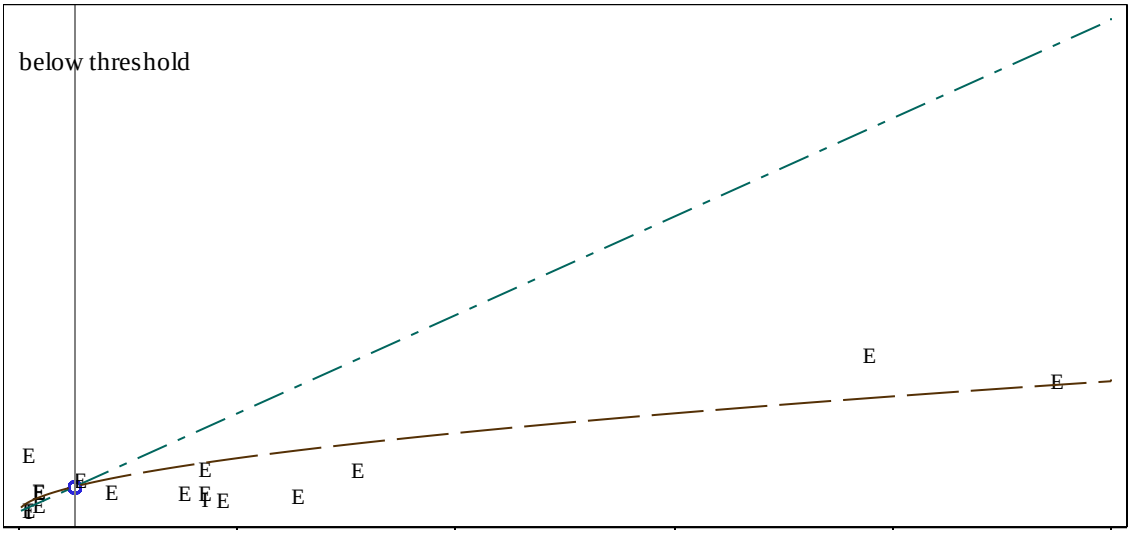

Figure 77. Threshold plot for Consumer Powder, Inhalation Concentration, Exc. ME 17

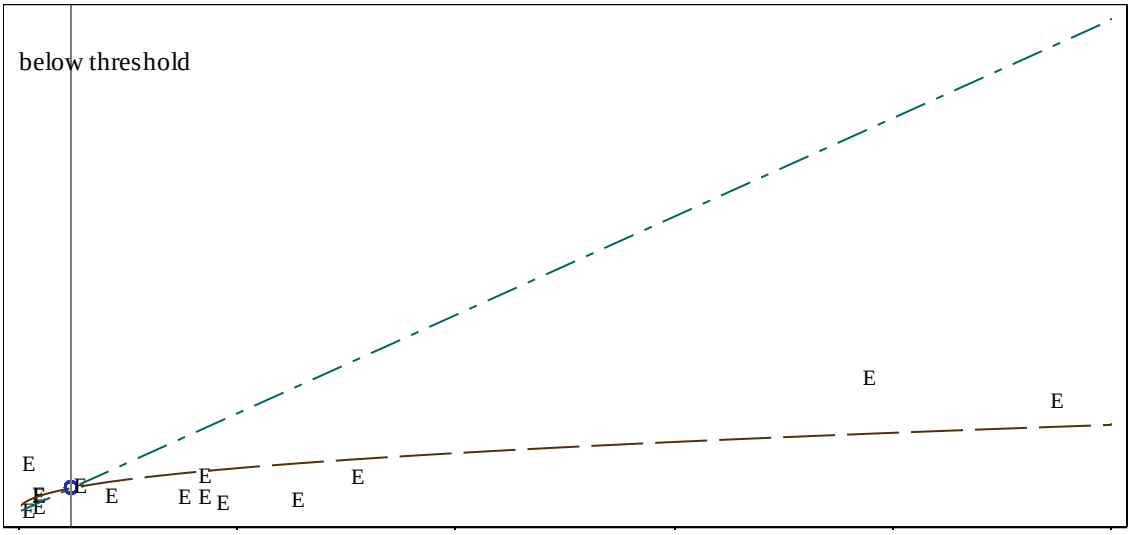

Figure 78. Threshold plot for Consumer Powder, Inhalation Concentration, Experienced consumers

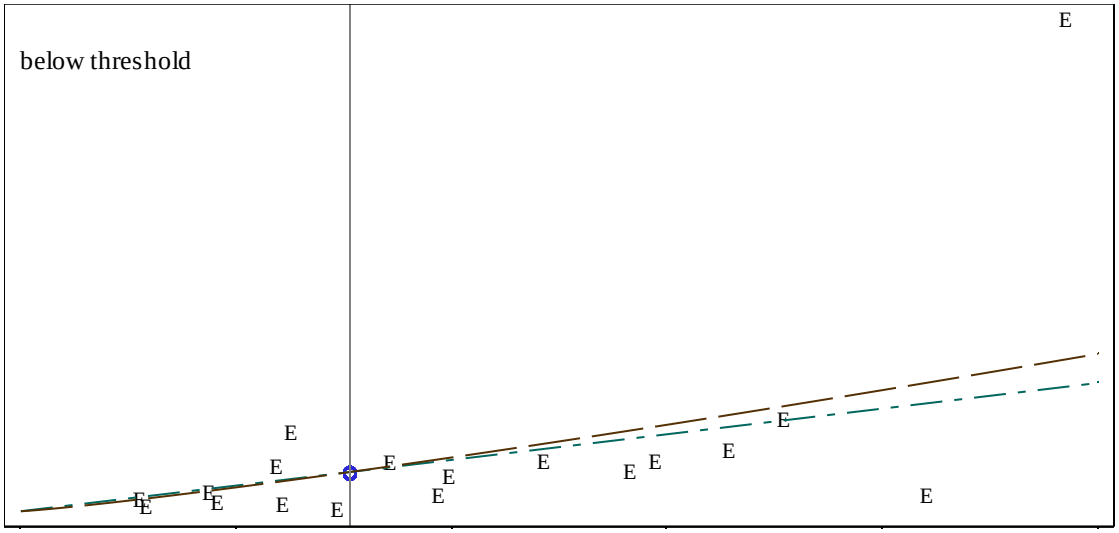

Figure 79. Threshold plot for Occupational Granules, Inhalation Concentration, All data

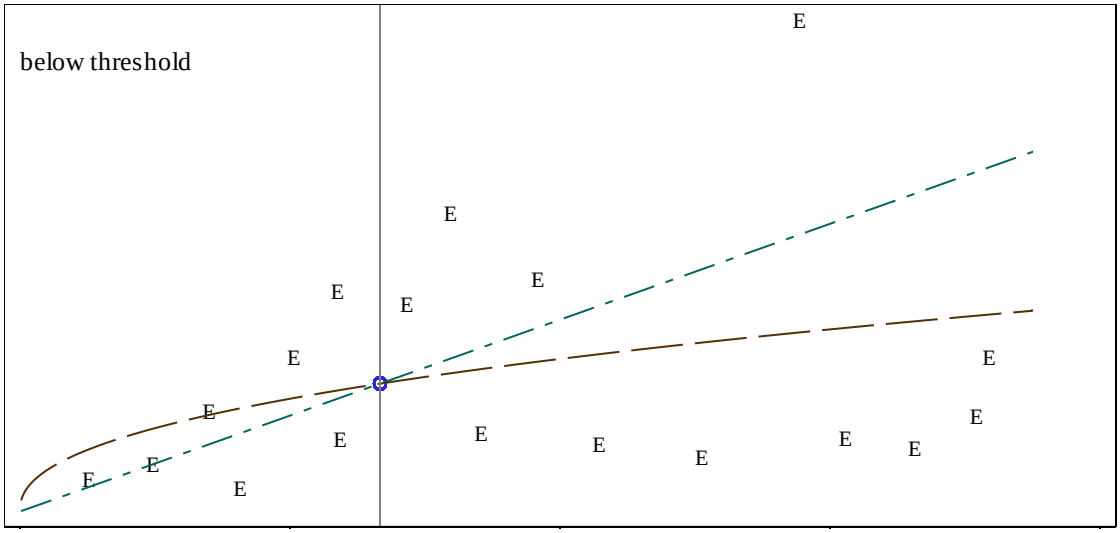

Figure 80. Threshold plot for Occupational Powder, Inhalation Concentration, All data

11. Alternative Statistical Approaches

Finally, we briefly discuss some alternative statistical approaches that were suggested by the HSRB (in their review of the solid pour study protocol) but we chose not to implement here.

For estimating the 95th percentile of the normalized or unit exposure, our preferred approach is to fit a lognormal statistical model. HSRB recommended consideration of a quantile regression approach, which would provide confidence intervals for the 95th percentile assuming a simple random sample from an unspecified distribution. This is exactly the same as the above calculations of the confidence intervals for P95s calculated using the non-parametric bootstrap approach (see Table 21 to Table 36). The quantile regression approach could also be applied to the exposure to estimate the 95th percentile of the exposure as a linear or non-linear function of the amount of active ingredient. We chose not to apply the latter approach due to its complexity and because it would not be consistent with the modeling approaches used for estimating the arithmetic mean.

For estimating the dependence of exposure on the amount of active ingredient, our main model was the linear model described above, where the mean log(exposure) is a linear function of the log(amount of active ingredient). We also

considered a quadratic model, but found the quadratic term to be non-significant. The HSRB suggested including non-linear functions of the log-log-logistic or logistic forms:

Log-log-logistic: Exposure = $\delta + \frac{\alpha - \delta}{1 + \gamma \exp\{\beta \log(AI)\}}$ + Error.

3-parameter logistic: Exposure = $\frac{C}{1 + \exp\{\alpha + \beta \times AI\}}$ + Error.

Since there is no background exposure in most of these scenarios, we can usually assume δ = 0 for the log-log-logistic model. A major problem with using the log-log-logistic model is that the mean exposure is bounded above, which is possibly unrealistic. These models could be fitted using the SAS NLIN procedure. Since the linear model fitted the data reasonably well and is simpler to use, and also for consistency with the statistical analyses of previous scenarios, we chose not to apply these statistical models.